WEST Search History

DATE: Tuesday, October 15, 2002

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR			
L9	l5 near administ$4	0	L9
L8	L7 not l5	0	L8
L7	gpipld	1	L7
L6	gpi adj pld	14	L6
L5	((antibod? near (IPG or inositophosphoglycan$4)) or (GPI adj PLD))	22	L5
L4	((antibod? near (IPG or inositoplphosphoglycan$4)) or (GPI adj PLD))	22	L4
L3	L2 and GPI adj PLD	1	L3
L2	L1 and (IPG or (inositoplphosphoglycan$4))	33	L2
L1	(rademacher)[in] or (whitby)[in]	1303	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002

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L1          550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2           47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3           28 DUP REM L2 (19 DUPLICATES REMOVED)
L4            1 S L3 AND GPI-PLD
L5         1504 S  (IPG OR (INOSITOLPHOSPHOGLYCAN?))
L6            4 S L5    (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7            3 DUP REM L6 (1 DUPLICATE REMOVED)
L8           80 S L5 (10N) ANTIBOD?
L9           51 S L8 AND PD<19980327
L10          25 DUP REM L9 (26 DUPLICATES REMOVED)
L11        9525 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
L12         122 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?
L13          67 S L12 AND PD<19980327
L14          42 DUP REM L13 (25 DUPLICATES REMOVED)
L15           0 S L14 (10N) ADMINIST?
L16           0 S L14 (P) ADMINIST?
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WO 98 47565 A
98 11435

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 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985

 NEWS EXPRESS  October 14 CURRENT WINDOWS VERSION IS V6.01,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002

=>  file medline caplus embase biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:59:34 ON 15 OCT 2002

FILE 'CAPLUS' ENTERED AT 16:59:34 ON 15 OCT 2002
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FILE 'BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
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=> s rademacher t?/au or whitby h?/au
L1          550 RADEMACHER T?/AU OR WHITBY H?/AU

=> s l1 and (ipg or (inositolphosphoglycans))
L2           47 L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           28 DUP REM L2 (19 DUPLICATES REMOVED)

=> dis l3 1-28 ibib abs

L3   ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2002:10305  CAPLUS
DOCUMENT NUMBER:         136:64163
TITLE:                   Materials and methods relating for the treatment and
                         diagnosis of pre-eclampsia
INVENTOR(S):             Schofield, Julian; Rademacher, Thomas William
PATENT ASSIGNEE(S):      University College London, UK
SOURCE:                  PCT Int. Appl., 45 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.       KIND  DATE           APPLICATION NO.  DATE
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WO 2002000254 A2 20020103 WO 2001-GB2800 20010625
WO 2002000254 A3 20020530
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001074330 A5 20020108 AU 2001-74330 20010625
PRIORITY APPLN. INFO.: GB 2000-15625 A 20000626
WO 2001-GB2800 W 20010625

AB The present invention relates to use of GPI-PLD (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial GPI-PLD activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated GPI-PLD activity present in the placenta in pre-eclampsia may be correctable by administration of GPI-PLD to the mother to correct the problems caused by abnormal or dysregulated GPI-PLD, e.g. to reduce the abnormal release and in situ prodn. of placental **IPGs** (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous GPI-PLD or a fragment thereof, e.g. an inactive GPI-PLD capable of competing with or displacing the abnormal or dysregulated GPI-PLD, e.g. from Apo-A1.

L3 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833641 CAPLUS
DOCUMENT NUMBER: 135:354965
TITLE: Gelatin in assays, kits and lateral flow devices for determining inositol phosphoglycans and diagnosing pre-eclampsia
INVENTOR(S): Williams, Philip; Bord, Stephanie; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2001086292 A2 20011115 WO 2001-GB2082 20010511
WO 2001086292 A3 20020620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 2000-11590 A 20000512
GB 2001-2566 A 20010201

AB Assays, kits and methods for detg. the presence or amt. inositol phosphoglycans (**IPG**) analytes in samples are disclosed based on the finding that **IPG** antigens are capable of binding to gelatin. These assays can be used in the diagnosis of conditions where the presence or amt. of these analytes is a diagnostic marker for a condition. Methods for the diagnosis of pre-eclampsia, distinguishing different type of pre-eclampsia, are disclosed and also methods for detg. the onset of labor in a patient. An ELISA assay was developed using gelatin as the capture agent and rabbit polyclonal anti-**IPG** sera and a goat anti-rabbit horseradish peroxidase conjugated antibody as a two-component developing agent to analyze pre-eclamptic urine samples.

L3 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833334 CAPLUS
DOCUMENT NUMBER: 135:358109
TITLE: Preparation of inositol phosphoglycan derivatives as antidiabetics and **IPG** antagonists
INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Noberto; Francois, Irene
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE
WO 2001085747 A1 20011115 WO 2001-GB2093 20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2001053767 A1 20011220 US 2001-798125 20010302
PRIORITY APPLN. INFO.: GB 2000-11591 A 20000512
US 2000-203607P P 20000512
US 2001-798125 A 20010302

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (**IPG**), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic **IPG**

-P and/or IPG-A activities mentioned above to det. whether they will be suitable for use a IPG mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, O-(2-amino-2-deoxy-D-glucopyranosyl)-.beta.(1,6)-D-3-O-methyl-chiro-inositol was prepd. and used to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833333 CAPLUS
DOCUMENT NUMBER: 135:344674
TITLE: Preparation of inositol phosphoglycan derivatives as antidiabetics and IPG antagonists
INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Noberto; Francois, Irene
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085746	A1	20011115	WO 2001-GB2083	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001056072	A1	20011227	US 2001-798124	20010302

PRIORITY APPLN. INFO.: GB 2000-11592 A 20000512
US 2000-203599P P 20000512
US 2001-798124 A 20010302

AB Compds. X-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (IPG), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic IPG -P and/or IPG-A activities mentioned above to det. whether they will be suitable for use a IPG mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-inositol-1,2-cyclic phosphate was prepd. and used to treat a condition ameliorated by administration of and IPG second messenger or an IPG antagonist.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833332 CAPLUS
DOCUMENT NUMBER: 135:358108
TITLE: Preparation of inositol phosphoglycans as antidiabetics and IPG antagonists
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo Norberto; Francois, Irene; Martin-Lomas, Manuel
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085745	A1	20011115	WO 2001-GB2098	20010511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001041677	A1	20011115	US 2001-798004	20010302

PRIORITY APPLN. INFO.: GB 2000-11593 A 20000512
US 2000-203598P P 20000512
US 2001-798004 A 20010302

AB Compds. having a mimetic or antagonistic property of an inositol phosphoglycan Y-X-cyclitols wherein X and Y are sugar residue, cyclitol is substituted with phosphate, thiophosphate, phosphate ester, phosphonate, thiophosphate ester, thiophosphonate, phosphoramidite, phosphoramidate, cyclic phosphate, sulfur group, substituted hydroxyl group, halogen, and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an IPG second messenger or an IPG antagonist thereof. Preferred compds. of the invention are based on the substituted cyclitols, and in particular, the compds. are based on the linkage of two or more sugar residues to a cyclitol. Effect of these compds. on the activity of PDH phosphatase, PDH kinase, and acetyl CoA carboxylase I is reported. Thus, O-.alpha.-D-galactopyranosyl-(1-4)-(2-amino-2-deoxy-.alpha.-D-glucopyranosyl)-(1-6)-D-myo-inositol was prepd. and tested as antidiabetics and IPG antagonist.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:833327 CAPLUS
DOCUMENT NUMBER: 135:358107
TITLE: Preparation of inositol phosphates to treat a condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist
INVENTOR(S): Martin-Lomas, Manuel; **Rademacher, Thomas William**; Caro, Hugo Norbert; Francois, Irene
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085740	A2	20011115	WO 2001-GB2088	20010511
WO 2001085740	A3	20020328		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001051606	A1	20011213	US 2001-798005	20010302
AU 2001060426	A5	20011120	AU 2001-60426	20010511

PRIORITY APPLN. INFO.:

GB 2000-11594	A	20000512
US 2000-203596P	P	20000512
US 2001-798005	A	20010302
US 2000-203599P	P	20000512
WO 2001-GB2088	W	20010511

AB Compds. X-1,6-cyclitol wherein X is a sugar residue and cyclitol is (un)-substituted with phosphoryl, sulfur, amino, hydroxyl, halogen, and having a mimetic or antagonistic property of an inositolphosphoglycan (**IPG**), and the uses of these compds. are disclosed, together with the use, e.g. to treat a condition ameliorated by administration of an **IPG** second messenger or an **IPG** antagonist thereof. In particular, the compds. are based on the 1,6 linkage of a sugar residue and a cyclitol. Preferred compds. of the invention are based on the substituted cyclitols, and in particular cyclitols linked to a sugar moiety where the mol. is substituted with a neg. charged group such as phosphate. The compds. of the invention can be tested for one or more the characteristic **IPG**-P and/or **IPG**-A activities mentioned above to det. whether they will be suitable for use a **IPG** mimetics or antagonists. Preferred assays measure the effect of the compds. on PDH phosphatase, PKA or lipogenesis. The compds. can also be tested to det. whether they activate or inhibit other enzymes involved in insulin signaling mechanism, such as glucose-6-phosphatase. Thus, 1'-D-6-O-(2'-amino-4'-O-phosphate-2'-deoxy-.alpha.-D-glucopyranosyl)-myo-inositol-1,2-cyclic phosphate was prepd. and used to treat a condition ameliorated by administration of and **IPG** second messenger or an **IPG** antagonist.

L3 ANSWER 7 OF 28 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001412385 MEDLINE
DOCUMENT NUMBER: 21354778 PubMed ID: 11461192
TITLE: Reversal of type 2 diabetes in mice by products of malaria parasites. II. Role of inositol phosphoglycans (**IPGs**).
AUTHOR: Elased K M; Gumaa K A; de Souza J B; Rahmoune H; Playfair J H; **Rademacher T W**
CORPORATE SOURCE: Rademacher Group Ltd, Arthur Stanley House, 6th Floor, 40-50 Tottenham Street, London W1P 9PG, United Kingdom.. Khalid.elased@rademacher.co.uk
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2001 Jul) 73 (3) 248-58.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB We have previously shown that infection with Plasmodium yoelii malaria or injection of extracts from malaria-parasitized red cells induces hypoglycemia in normal mice and normalizes the hyperglycemia in mice made moderately diabetic with streptozotocin. Inositol phosphoglycans (**IPGs**) are released outside cells by hydrolysis of membrane-bound glycosylphosphatidylinositols (GPIs), and act as second messengers mediating insulin action. The C57BL/Ks-db/db and C57BL/6J-ob/ob mice offer good models for studies on human obesity and Type 2 diabetes. In the present study, we show that a single iv injection of **IPG**-A or **IPG**-P extracted from P. yoelii significantly ($P < 0.02$) lowers the blood glucose in STZ-diabetic, db/db, and in ob/ob mice for at least 4--6 h. Using rat white adipocytes, **IPG**-P increased lipogenesis by 20--30% in the presence and absence of maximal concentrations of insulin (10(-8) M) ($P < 0.01$) and stimulated pyruvate dehydrogenase (PDH) phosphatase in a dose-related manner. Both **IPG**-A and **IPG**-P inhibited c-AMP-dependent protein kinase (PKA) in a dose-related manner. Compositional analysis of **IPGs** after 24 h hydrolysis revealed the presence of myo-inositol, phosphorus, galactosamine, glucosamine, and glucose in both **IPG**-A and **IPG**-P. However, hydrolysis of **IPGs** for 4 h highlighted differences between **IPG**-A and **IPG**-P. There are some functional similarities between P. yoelii **IPGs** and those previously described for mammalian liver. However, this is the first report of the hypoglycemic effect of **IPGs** in murine models of Type 2 diabetes. We suggest that **IPGs** isolated from P. yoelii, when fully characterized, may provide structural information for the synthesis of new drugs for the management of diabetes mellitus.

L3 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:911091 CAPLUS

DOCUMENT NUMBER: 134:37032
TITLE: Adenosine diphosphatase and activators thereof and their therapeutic and diagnostic uses for preeclampsia and platelet aggregation-associated conditions
INVENTOR(S): McLean, Patricia; Greenbaum, Leslie; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078330	A2	20001228	WO 2000-GB2333	20000616
WO 2000078330	A3	20010525		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1185295	A2	20020313	EP 2000-940550	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1999-14326 A 19990618
WO 2000-GB2333 W 20000616

AB Materials and methods are provided for the diagnosis and treatment of preeclampsia and related conditions characterized by platelet aggregation. Adenosine diphosphatase (ADPase) and activators of ADPase are used for the treatment of preeclampsia, in order to overcome the inhibition of ADPase by inositol phosphoglycans (**IPGs**). Also provided is a method for screening for compds. with ADPase-stimulatory activity in the presence or absence of **IPGs**.

L3 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:457304 CAPLUS
DOCUMENT NUMBER: 133:55669
TITLE: Treatment and diagnosis of cancer using **inositolphosphoglycans** antagonists
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039589	A1	20000706	WO 1999-GB4382	19991223
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141723	A1	20011010	EP 1999-962426	19991223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533475	T2	20021008	JP 2000-591437	19991223

PRIORITY APPLN. INFO.: GB 1998-28564 A 19981223
WO 1999-GB4382 W 19991223

AB **Inositolphosphoglycans** (**IPGs**), and in particular A-type substances comprising myo-inositol, are tumor autocrine factors (TAFs), that is factors which cause tumor cell proliferation. The use of A-type **IPG** antagonists for the treatment of cancer and a method for the diagnosis or prognosis of cancer based on the presence or amt. of **IPGs** in a sample from a patient is disclosed.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15024 CAPLUS
DOCUMENT NUMBER: 132:59168
TITLE: Inositolphosphoglycan and ribose for treatment of ischemia-reperfusion injury
INVENTOR(S): **Rademacher, Thomas William**; Greenbaum, Leslie; McLean, Patricia
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000000205	A1	20000106	WO 1999-GB1499	19990512
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9939402	A1	20000117	AU 1999-39402	19990512
AU 748892	B2	20020613		
EP 1091743	A1	20010418	EP 1999-922293	19990512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

JP 2002519328 T2 20020702 JP 2000-556790 19990512
PRIORITY APPLN. INFO.: GB 1998-14039 A 19980629
WO 1999-GB1499 W 19990512

AB Compns. comprising **inositolphosphoglycans** (**IPGs**) and ribose are disclosed, and their use in the prevention or treatment of ischemic-reperfusion injury. This treatment increases the energy generating systems of cells by employing the mitochondrial oxidative restoration system. The use of the compns. in preserving organs for transplantation is also disclosed.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 28 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2000513875 MEDLINE
DOCUMENT NUMBER: 20522979 PubMed ID: 11072827
TITLE: Inositolphosphoglycan mediators structurally related to glycosyl phosphatidylinositol anchors: synthesis, structure and biological activity.
AUTHOR: Martin-Lomas M; Khiar N; Garcia S; Koessler J L; Nieto P M; **Rademacher T W**
CORPORATE SOURCE: Grupo de Carbohidratos, Instituto de Investigaciones Quimicas CSIC-UNSE, Sevilla, Spain.. manuel.martin-lomas@iiq.cartuja.csic.es
SOURCE: CHEMISTRY, (2000 Oct 2) 6 (19) 3608-21.
Journal code: 9513783. ISSN: 0947-6539.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001128

AB The preparation of the pseudopentasaccharide 1a, an inositol-phosphoglycan (**IPG**) that contains the conserved linear structure of glycosyl phosphatidylinositol anchors (GPI anchors), was carried out by using a highly convergent 2+3-block synthesis approach which involves imidate and sulfoxide glycosylation reactions. The preferred solution conformation of this structure was determined by using NMR spectroscopy and molecular dynamics simulations prior to carrying out quantitative structure--activity relationship studies in connection with the insulin signalling process. The ability of 1a to stimulate lipogenesis in rat adipocytes as well as to inhibit cAMP dependent protein kinase and to activate pyruvate dehydrogenase phosphatase was investigated. Compound 1a did not show any significant activity, which may be taken as a strong indication that the GPI anchors are not the precursors of the **IPG** mediators.

L3 ANSWER 12 OF 28 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000188034 MEDLINE
DOCUMENT NUMBER: 20188034 PubMed ID: 10720442
TITLE: Inositol phosphoglycans and signal transduction systems in pregnancy in preeclampsia and diabetes: evidence for a significant regulatory role in preeclampsia at placental and systemic levels.
AUTHOR: Kunjara S; Greenbaum A L; Wang D Y; Caro H N; McLean P; Redman C W; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, The Windeyer Building, 46, University College London Medical School, Cleveland Street, London, W1P 6DB, England.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 Feb) 69 (2) 144-58.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000606
Last Updated on STN: 20000606
Entered Medline: 20000519

AB Measurements have been made of the urinary content of inositol phosphoglycans **IPG** P-type and **IPG** A-type, putative insulin second messengers, in preeclampsia, in type I insulin-treated diabetic pregnant women and their matched control subjects, and nonpregnant women of child-bearing age. The content of **IPG** P-type and **IPG** A-type was also measured in the placenta from preeclamptic patients and from normal pregnancies. Pregnancy was associated with an increase, approximately twofold, in urinary output of **IPG**-P-type relative to nonpregnant controls ($P<0.01$). The 24-h output of **IPG** P-type in urine in preeclamptic women was significantly higher (2- to 3-fold) than in pregnant control subjects matched for age, parity, and stage of gestation ($P<0.02$). In contrast, insulin-dependent diabetic pregnant women did not show any significant change in urinary output of **IPG** P-type or **IPG** A-type relative to pregnant control subjects. Evidence for a possible relationship and correlation between the urinary excretion of **IPG** P-type and markers of preeclampsia, including proteinuria ($r = 0.720$, $P<0.01$), plasma aspartate transaminase ($r = 0.658$, $P<0.05$), and platelet counts ($r = 0.613$, $P<0.05$) is presented. A high yield of **IPG** P-type was extracted from human placenta, in preeclampsia some 3-fold higher ($P = 0.03$) than the normal value, whereas no **IPG** A-type (with lipogenic-stimulating activity) was found. Low concentrations of placental **IPG** A-type were detected relative to **IPG** P-type using assay systems dependent upon the effect of this mediator on cAMP-dependent protein kinase or on a proliferation assay using thymidine incorporation into DNA of EGFR T17 fibroblasts. It is postulated that the high urinary excretion **IPG** P-type in preeclampsia reflects high placental levels and relates to the accumulation of glycogen in the placenta. The paracrine effects of placental **IPG** P-type (stimulation off other endocrine glands and/or endothelial cells) could contribute to the pathogenesis of the maternal syndrome. A possible theoretical link between elevated placental **IPG** P-type and apoptosis is proposed.

L3 ANSWER 13 OF 28 BIOSIS
ACCESSION NUMBER: 2001:50486 BIOSIS
DOCUMENT NUMBER: PREV200100050486
TITLE: Inositol phosphoglycans (**IPGS**) derived from Plasmodium yoelii mimic insulin action in vivo.
AUTHOR(S): Elased, K. M. (1); Gumaa, K. A. (1); de Souza, J. B.; **Rademacher, T. W.**

CORPORATE SOURCE: (1) Rademacher Group Ltd, 40-50 Tottenham Street, Arthur Stanley House, 6th Floor, London, W1P 9PG UK
SOURCE: Journal of Endocrinology, (November, 2000) Vol. 167, No. Supplement, pp. P62. print.
Meeting Info.: 191st Meeting of the Society for Endocrinology London, England, UK November 20-21, 2000 Society for Endocrinology
. ISSN: 0022-0795.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L3 ANSWER 14 OF 28 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000295348 MEDLINE
DOCUMENT NUMBER: 20295348 PubMed ID: 10833332
TITLE: Inositol phosphoglycans and the regulation of the secretion of leptin: in vitro effects on leptin release from adipocytes and the relationship to obesity.
AUTHOR: Kunjara S; Wang D Y; McLean P; Greenbaum A L; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, UK.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (2000 May) 70 (1) 61-8. Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20000728
Entered Medline: 20000719

AB The ratio of two families of inositol phosphoglycans (**IPG**-A: **IPG**-P), insulin second messengers, is raised in non-insulin-dependent diabetes mellitus (NIDDM) and obesity. It is shown here that **IPG** A type inhibits leptin release from adipocytes, contrasting with the action of insulin (stimulation) and **IPG** P type (no effect). The significance of inhibitory effects of **IPG** A type on leptin release is important in relation to obesity and NIDDM in view of the action of leptin in promoting Lep expression and fat oxidation in muscle, in addition to its effects on satiety. Energy conservation and oxidation via interorgan regulation by leptin could be compromised by a rise in the **IPG**-A:**IPG**-P ratio.

L3 ANSWER 15 OF 28 CAPLUS
ACCESSION NUMBER: 1999:640696 CAPLUS
DOCUMENT NUMBER: 131:256346
TITLE: Antagonism of inositolphosphoglycan signaling in mast cells, basophils and eosinophils
INVENTOR(S): **Rademacher, Thomas William**; **Whitby, Helen**
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949855	A2	19991007	WO 1999-GB981	19990329
WO 9949855	A3	19991118		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319588	AA	19991007	CA 1999-2319588	19990329
AU 9931596	A1	19991018	AU 1999-31596	19990329
EP 1066043	A2	20010110	EP 1999-913481	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-6645 A 19980327
WO 1999-GB981 W 19990329

AB The authors disclose that **inositolphosphoglycans** (**IPGs**) can be obtained from basophils, eosinophils and mast cells and that allergen stimulation of these cells results in **IPG** release. **IPGs**, acting as second messengers in non-allergen stimulated cells, induced histamine release or degranulation. Thus, **IPG** antagonists are envisioned for the treatment of conditions (esp. allergy and asthma) mediated by the release of **IPGs** from mast cells, basophils or eosinophils. Preferred **IPG** antagonists include anti-**IPG** antibodies, inhibitors of the enzyme glycosylphosphatidylinositol phospholipase D, and competitive antagonists.

L3 ANSWER 16 OF 28 CAPLUS
ACCESSION NUMBER: 1999:614255 CAPLUS
DOCUMENT NUMBER: 131:237961
TITLE: Materials and methods using antibody binding for identifying inositolphosphoglycan mimetics
INVENTOR(S): **Rademacher, Thomas William**; Williams, Phillip
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947926	A2	19990923	WO 1999-GB845	19990318
WO 9947926	A3	19991104		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,				

MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2321734	AA	19990923	CA 1999-2321734	19990318	
AU 9929468	A1	19991011	AU 1999-29468	19990318	
EP 1066521	A2	20010110	EP 1999-910536	19990318	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002507724	T2	20020312	JP 2000-537070	19990318	
PRIORITY APPLN. INFO.:			GB 1998-5771	A	19980318
			WO 1999-GB845	W	19990318

AB Methods for detg. a binding profile for an inositolphosphoglycan (**IPG**) or a candidate mimetic compd. are disclosed in which the **IPG** or candidate mimetic compd. is contacted with an anti-**IPG** antibody in a binding assay and the binding of the **IPG** or candidate mimetic compd. to the antibody is used to establish the binding profiles. The profiles are then used in methods for identifying candidate compds. for further testing or development as **IPG** mimetics, providing lead compds. for further development as pharmaceuticals.

L3 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:613973 CAPLUS
DOCUMENT NUMBER: 131:241984
TITLE: Anti-inositolphosphoglycan monoclonal antibodies
INVENTOR(S): Nieto, Isabel Varela; Mato, Jose; Prieto, Jesus; Williams, Phillip; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9947565	A1	19990923	WO 1999-GB844	19990318	
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2321113	AA	19990923	CA 1999-2321113	19990318	
AU 9929467	A1	19991011	AU 1999-29467	19990318	
AU 748080	B2	20020530			
EP 1062246	A1	20001227	EP 1999-910535	19990318	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002506631	T2	20020305	JP 2000-536756	19990318	
PRIORITY APPLN. INFO.:			GB 1998-5739	A	19980318
			GB 1998-11000	A	19980521
			WO 1999-GB844	W	19990318

AB The present invention relates to anti-**IPG** antibodies, and in particular monoclonal antibodies produced by hybridoma cell lines 2F7, 2D1 and 5H6, and the use of these and other similar antibodies in the treatment and diagnosis of pre-eclampsia or diabetes, esp. type I diabetes. A method of producing anti-**IPG** antibodies by immunizing an animal with **IPG** unconjugated to an immunogenic carrier is also disclosed.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:495179 CAPLUS
DOCUMENT NUMBER: 131:125475
TITLE: Neurotrophic properties of **IPGs** and **IPG** analogues
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo Norberto; Martin-Lomas, Manuel; Nieto, Isabel Varela; Alvarez, Yolanda Leon
PATENT ASSIGNEE(S): Rademacher Group Limited, UK
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9938516	A1	19990805	WO 1998-GB3847	19981221	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2318584	AA	19990805	CA 1998-2318584	19981221	
AU 9917708	A1	19990816	AU 1999-17708	19981221	
EP 1064003	A1	20010103	EP 1998-962574	19981221	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002501899	T2	20020122	JP 2000-529249	19981221	
PRIORITY APPLN. INFO.:			GB 1998-1899	A	19980129
			WO 1998-GB3847	W	19981221

AB **Inositolphosphoglycans** (**IPGs**) or inositol-contg. **IPG** analogs can be used to specifically cause neuron proliferation or neuron differentiation, and in particular neurite outgrowth. P-type **IPGs** or chiro-inositol contg. analogs cause neurite outgrowth and A-type **IPGs** or myo-inositol contg. analogs cause neuron proliferation. Compns. comprising these agents and their medical uses are also disclosed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 28 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2000076804 MEDLINE
DOCUMENT NUMBER: 20076804 PubMed ID: 10607479
TITLE: Inositol phosphoglycans in diabetes and obesity: urinary levels of **IPG** A-type and **IPG** P-type, and relationship to pathophysiological changes.
AUTHOR: Kunjara S; Wang D Y; Greenbaum A L; McLean P; Kurtz A; **Rademacher T W**
CORPORATE SOURCE: Department of Molecular Pathology, Molecular Medicine Unit, University College London Medical School, The Windeyer Building, 46, Cleveland Street, London, W1P 6DB, United Kingdom.
SOURCE: MOLECULAR GENETICS AND METABOLISM, (1999 Dec) 68 (4) 488-502.
Journal code: 9805456. ISSN: 1096-7192.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000301

AB Measurements have been made, in adult male diabetic patients and control subjects, of the urinary content of inositol phosphoglycans (**IPGs**), the **IPG** A-type and **IPG** P-type forms, which, among other actions, regulate pathways of glucose utilization, lipogenesis, triglyceride formation, and pyruvate dehydrogenase (PDH) activity. Urine samples from the entire diabetic group showed a 2- to 3-fold increase in **IPG** A-type, and a fall in the **IPG** P-type:**IPG** A-type ratio relative to the control group. Subdivision of the diabetic patients into lean IDDM and obese NIDDM groups revealed significant differences in the **IPG** P-type:**IPG** A-type ratio between these groups, this ratio decreasing with increases in the body mass index (BMI). Analysis of the relationships among **IPGs** and HbA1, blood pressure, and BMI indicated that a fall in the **IPG** P-type: **IPG** A-type ratio correlated with a rise in the HbA1 (indicative of impaired glycemic control), with increased systolic blood pressure and increased obesity, all factors linked to Syndrome X. There was a parallism between the profile of the **IPG** P-type:**IPG** A-type ratio and the well-established pattern of insulin resistance and BMI. In vitro studies of the effects of alterations in the **IPG** P-type: **IPG** A-type ratio on the activation of the pyruvate dehydrogenase complex (PDH complex) at the PDH phosphatase reaction demonstrated that **IPG** A-type forms antagonized the stimulation of the PDH phosphatase by **IPG** P-type forms, thus having a negative effect on the conversion of PDH to the active, dephosphorylated, form. This observation could provide a mechanism whereby the shifts in the **IPG** P-type:**IPG** A-type ratio reported above could change the metabolic pattern from one directed to glucose oxidation to one more directed toward energy conservation and lipid storage.

L3 ANSWER 20 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393699 BIOSIS
DOCUMENT NUMBER: PREV199900393699
TITLE: Higher detection of **inositolphosphoglycans** (**IPG**) in pre-eclamptic than in normal placenta by immunohistochemical staining.
AUTHOR(S): Deborde, S. (1); Sooranna, S. R.; Williams, P. J. (1); Mato, J.; **Rademacher, T. W. (1)**
CORPORATE SOURCE: (1) Molecular Medicine Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.21. Meeting Info.: 5th Conference of the International Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 21 OF 28 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:393697 BIOSIS
DOCUMENT NUMBER: PREV199900393697
TITLE: Investigation of **inositolphosphoglycans** (**IPG**) activity in the brush border membrane of normal and pre-eclamptic (PE) human placenta.
AUTHOR(S): Deborde, S. (1); Kunjara, S. (1); **Rademacher, T. W. (1)**
CORPORATE SOURCE: (1) Mol Med Unit, Department of Molecular Pathology, UCL, London UK
SOURCE: Placenta, (July-Aug., 1999) Vol. 20, No. 5-6, pp. A.20. Meeting Info.: 5th Conference of the International Federation of Placenta Associations and the 8th Meeting of the European Placenta Group Schladming, Austria September 26-29, 1999 European Placenta Group . ISSN: 0143-4004.
DOCUMENT TYPE: Conference
LANGUAGE: English

L3 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:184077 CAPLUS
DOCUMENT NUMBER: 128:226252
TITLE: Materials and methods using P- and A-type **inositolphosphoglycans** and their antagonists for the diagnosis and treatment of diabetes and associated obesity
INVENTOR(S): **Rademacher, Thomas William**; McLean, Patricia
PATENT ASSIGNEE(S): Hoeft Rademacher Limited, UK; Rademacher, Thomas William; McLean, Patricia
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9811435	A1	19980319	WO 1997-GB2440	19970911	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9741304	A1	19980402	AU 1997-41304	19970911	
AU 722425	B2	20000803			
EP 925503	A1	19990630	EP 1997-939083	19970911	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1234118	A	19991103	CN 1997-199097	19970911	
BR 9711753	A	20000118	BR 1997-11753	19970911	
JP 2001505658	T2	20010424	JP 1998-513366	19970911	
PRIORITY APPLN. INFO.:			GB 1996-18934	A	19960911
			WO 1997-GB2440	W	19970911

AB The diagnosis of diabetes based on the level or ratio of P- and A-type **inositolphosphoglycans** (**IPGs**) in a sample from a patient, and the use of P- and A-type **IPGs** or their antagonists in the treatment of diabetes, are disclosed. In particular, the invention provides treatment of IDDM or lean type II diabetes (NIDDM) with a mixt. of P- and A-type mediators, and treatment of obese type II diabetes (NIDDM) with a P-type mediator and/or an A-type antagonist.

L3 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180889 CAPLUS
DOCUMENT NUMBER: 128:240997
TITLE: Cyclitol containing carbohydrates from human tissue which regulate glycogen metabolism and their use in pharmaceuticals
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9811117	A1	19980319	WO 1997-GB2533	19970911	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9743101	A1	19980402	AU 1997-43101	19970911	
AU 713100	B2	19991125			
EP 925304	A1	19990630	EP 1997-919168	19970911	
EP 925304	B1	20000426			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 192160	E	20000515	AT 1997-919168	19970911	
ES 2147988	T3	20001001	ES 1997-919168	19970911	
JP 2001500859	T2	20010123	JP 1998-513410	19970911	
US 6271204	B1	20010807	US 1999-254748	19990614	
PRIORITY APPLN. INFO.:			GB 1996-18929	A	19960911
			WO 1997-GB2533	W	19970911

AB The application relates to the purifn. and characterization of a family of P-type **inositolphosphoglycans** (**IPGs**) from human liver and placenta. These substances are shown to have P-type biol. activity, e.g., activating pyruvate dehydrogenase (PDH) phosphatase. The characterization of the compds. demonstrates that they contain metal ions, in particular Mn2+ and/or Zn2+, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g., for the treatment of diabetes, and in screening for synthetic analogs.

L3 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180888 CAPLUS
DOCUMENT NUMBER: 128:242350
TITLE: A type A glycosylphosphatidylinositol second messenger from human tissue involve in regulation of lipogenesis
INVENTOR(S): **Rademacher, Thomas William**; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9811116	A1	19980319	WO 1997-GB2444	19970911	
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9741307	A1	19980402	AU 1997-41307	19970911	
AU 713103	B2	19991125			
EP 925305	A1	19990630	EP 1997-939087	19970911	
EP 925305	B1	20000426			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 192161	E	20000515	AT 1997-939087	19970911	
ES 2147996	T3	20001001	ES 1997-939087	19970911	
JP 2001504450	T2	20010403	JP 1998-513368	19970911	
US 6303580	B1	20011016	US 1999-254797	19990604	
US 2001039027	A1	20011108	US 2001-775856	20010201	
PRIORITY APPLN. INFO.:			GB 1996-18930	A	19960911

WO 1997-GB2444 W 19970911
US 1999-254797 A3 19990604

AB A family of A-type **inositolphosphoglycans** (**IPGs**) from human liver and placenta that appear to play a role in the regulation of lipogenesis are identified and characterized. These substances have the biol. activity assocd. with A-type **IPG** fractions, namely regulating lipogenic activity and inhibiting cAMP dependent protein kinase. The characterization of the compds. demonstrates that they contain metal ions, in particular Zn2+, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g. for the treatment of diabetes, and in screening for synthetic analogs.

L3 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180785 CAPLUS
DOCUMENT NUMBER: 128:226268
TITLE: P-type **inositolphosphoglycans** and antagonists thereof in diagnosis and treatment of pre-eclampsia and diabetes
INVENTOR(S): **Rademacher, Thomas William**; Mclean, Patricia
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Mclean, Patricia
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810791	A1	19980319	WO 1997-GB2534	19970911
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743102	A1	19980402	AU 1997-43102	19970911
AU 715884	B2	20000210		
EP 939651	A1	19990908	EP 1997-919169	19970911
EP 939651	B1	20000531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1235556	A	19991117	CN 1997-199318	19970911
BR 9711752	A	20000118	BR 1997-11752	19970911
AT 193452	E	20000615	AT 1997-919169	19970911
ES 2148967	T3	20001016	ES 1997-919169	19970911
JP 2001501598	T2	20010206	JP 1998-513411	19970911

PRIORITY APPLN. INFO.: GB 1996-18931 A 19960911
WO 1997-GB2534 W 19970911

AB The invention relates to materials and methods for the diagnosis and treatment of pre-eclampsia, and more particularly to the role of P-type **inositolphosphoglycans** (**IPGs**) in the occurrence of pre-eclampsia. Methods of diagnosing pre-eclampsia by detg. the level of P-type **IPGs** and uses of antagonists of P-type **IPGs** in the treatment of pre-eclampsia are disclosed, together with a method for screening for P-type **IPG** antagonists.

L3 ANSWER 26 OF 28 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 97406564 MEDLINE
DOCUMENT NUMBER: 97406564 PubMed ID: 9259987
TITLE: Isolation and partial characterisation of insulin-mimetic inositol phosphoglycans from human liver.
AUTHOR: Caro H N; Kunjara S; **Rademacher T W**; Leon Y; Jones D R; Avila M A; Varela-Nieto I
CORPORATE SOURCE: Department of Molecular Pathology, University College London Medical School, United Kingdom.
SOURCE: BIOCHEMICAL AND MOLECULAR MEDICINE, (1997 Aug) 61 (2) 214-28.
Journal code: 9508702. ISSN: 1077-3150.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY DATE: Entered STN: 19971105
Last Updated on STN: 20000303
Entered Medline: 19971023

AB Extracts of human liver were found to contain activities which copurified and coeluted with the two major subtypes of mediators (type A and type P) isolated from insulin-stimulated rat liver. The putative type A mediator from human liver inhibited cAMP-dependent protein kinase from bovine heart, decreased phosphoenolypyruvate carboxykinase mRNA levels in rat hepatoma cells, and stimulated lipogenesis in rat adipocytes. The putative type P mediator stimulated bovine heart pyruvate dehydrogenase phosphatase. Both fractions were able to stimulate proliferation of EGFR T17 fibroblasts and the type A was able to support growth in organotypic cultures of chicken embryo cochleovestibular ganglia. Both activities were resistant to Pronase treatment and the presence of carbohydrates, phosphate, and free-amino groups were confirmed in the two fractions. These properties are consistent with the structure/ function characteristics of the type A and P **inositolphosphoglycans** (**IPG**) previously characterized from rat liver. Further, the ability of the human-derived mediators to interact with rat adipocytes and bovine-derived metabolic enzymes suggests similarity in structure between the mediators purified from different species. Galactose oxidase-susceptible membrane-associated glycosylphosphatidylinositols (GPI) have been proposed to be the precursors of **IPG**. GPI was purified from human liver membranes followed by treatment with galactose oxidase and reduction with NaB3H4. Serial t.l.c. revealed three radiolabeled bands which comigrated with the putative GPI precursors found in rat liver. These galactose-oxidase-reactive lipidic compounds, however, were only partially susceptible to hydrolysis with phosphatidylinositol-specific phospholipase C from Bacillus thuringiensis and were resistant to glycosylphosphatidylinositol-specific phospholipase C from Trypanosoma brucei. These data indicate that **IPG** molecules with insulin-like biological activities are present in human liver.

L3 ANSWER 27 OF 28 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96333396 MEDLINE
DOCUMENT NUMBER: 96333396 PubMed ID: 8757890

TITLE: Structural similarities among malaria toxins insulin second messengers, and bacterial endotoxin.
AUTHOR: Caro H N; Sheikh N A; Taverne J; Playfair J H; **Rademacher T W**
CORPORATE SOURCE: Molecular Medicine Unit, Department of Molecular Pathology, University College London Medical School, United Kingdom.
SOURCE: INFECTION AND IMMUNITY, (1996 Aug) 64 (8) 3438-41. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19961008
Last Updated on STN: 19970203
Entered Medline: 19960926

AB Malaria toxin causes hypoglycemia and induction of tumor necrosis factor. Extracts of parasitized erythrocytes which were coeluted and copurified with one of the two subtypes of mammalian insulin-mimetic **inositolphosphoglycans** similarly induced fibroblast proliferation in the absence of serum. In addition, induction of tumor necrosis factor in macrophages by malaria toxin and by lipopolysaccharide from Escherichia coli was enhanced by pretreatment of these toxins with alpha-galactosidase. Thus, parasitized erythrocytes contain both soluble inositolphosphoglycan-like insulin second messengers and endotoxin-like lipidic molecules.

L3 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:315887 CAPLUS
DOCUMENT NUMBER: 120:315887
TITLE: Inositolphosphoglycan second messengers
AUTHOR(S): **Rademacher, T. W.**; Caro, H.; Kunjara, S.; Wang, D. Y.; Greenbaum, A. L.; McLean, P.
CORPORATE SOURCE: Dep. Mol. Pathol., Univ. Coll. London Med. Sch., London, W1P 6DB, UK
SOURCE: Brazilian Journal of Medical and Biological Research (1994), 27(2), 327-41
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 77 refs., of the role of inositolphosphoglycan (**IPG**) in signal transduction by growth factors with special emphasis on insulin and insulin-like factors. Specific topics discussed were: origin of the **IPG** precursors-glycosylphosphatidylinositol glycans, viz. target cell synthesis vs. circulating hormone vs. membrane-anchored protein; location of **IPG** generation; relationship to the novel calcium-influx factors; relationship to the insulin-mimetics derived from malarial toxic antigen; relationship to tyrosine kinases and G-proteins; enzymes involved in cell surface GPI hydrolysis; and structure of **IPGs**.

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)

=> s l3 and GPI-PLD
L4 1 L3 AND GPI-PLD

=> dis l4 ibib abs kwic

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10305 CAPLUS
DOCUMENT NUMBER: 136:64163
TITLE: Materials and methods relating for the treatment and diagnosis of pre-eclampsia
INVENTOR(S): Schofield, Julian; **Rademacher, Thomas William**
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000254	A2	20020103	WO 2001-GB2800	20010625
WO 2002000254	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001074330	A5	20020108	AU 2001-74330	20010625

PRIORITY APPLN. INFO.: GB 2000-15625 A 20000626
WO 2001-GB2800 W 20010625

AB The present invention relates to use of **GPI-PLD** (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial **GPI-PLD** activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated **GPI-PLD** activity present in the placenta in pre-eclampsia may be correctable by administration of **GPI-PLD** to the mother to correct the problems caused by abnormal or dysregulated **GPI-PLD**, e.g. to reduce the abnormal release and in situ prodn. of placental **IPGs** (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous **GPI-PLD** or a fragment thereof, e.g. an inactive **GPI-PLD** capable of competing with or displacing the abnormal or dysregulated **GPI-PLD**, e.g. from Apo-A1.

IN Schofield, Julian; **Rademacher, Thomas William**

AB The present invention relates to use of **GPI-PLD** (glycosylphosphatidylinositol phospholipase D) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial **GPI-PLD** activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated **GPI-PLD** activity present in the placenta in pre-eclampsia may be correctable by administration of **GPI-PLD** to the mother to correct the problems caused by abnormal or dysregulated **GPI-PLD**, e.g. to reduce the abnormal release and in situ prodn. of placental **IPGs** (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous **GPI-PLD** or a fragment thereof, e.g. an inactive **GPI-PLD** capable of competing with or displacing the abnormal or dysregulated **GPI-PLD**, e.g. from Apo-A1.

IT Apolipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A-I, **GPI-PLD** displacement from; materials and methods relating for the treatment and diagnosis of pre-eclampsia)

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD

=> s s (ipg or (inositolphosphoglycans))
MISSING OPERATOR 'S (IPG'
The search profile that was entered contains terms or nested terms that are not separated by a logical operator.

=> s (ipg or (inositolphosphoglycan?))
L5 1504 (IPG OR (INOSITOLPHOSPHOGLYCAN?))

=> s l5 (P) (GPI-PLD or (glycosylphosphatidylinositol phospholipase D)
UNMATCHED LEFT PARENTHESIS 'P) (GPI-PLD'
The number of right parentheses in a query must be equal to the number of left parentheses.

=> s l5 (P) (GPI-PLD or (glycosylphosphatidylinositol (1N) phospholipase D))
L6 4 L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSPHOLIPASE D))

=> dup rem l6
PROCESSING COMPLETED FOR L6
L7 3 DUP REM L6 (1 DUPLICATE REMOVED)

=> dis l7 1-3 ibib abs

L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10305 CAPLUS
DOCUMENT NUMBER: 136:64163
TITLE: Materials and methods relating for the treatment and diagnosis of pre-eclampsia
INVENTOR(S): Schofield, Julian; Rademacher, Thomas William
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000254	A2	20020103	WO 2001-GB2800	20010625
WO 2002000254	A3	20020530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001074330	A5	20020108	AU 2001-74330	20010625

PRIORITY APPLN. INFO.: GB 2000-15625 A 20000626
WO 2001-GB2800 W 20010625

AB The present invention relates to use of **GPI-PLD** (**glycosylphosphatidylinositol phospholipase D**) antagonists for the prevention, treatment and diagnosis of pre-eclampsia. The substantial **GPI-PLD** activity is present in the placenta in pre-eclampsia is not expressed in the placenta, but rather is taken up from the maternal circulation. As a result, abnormal or dysregulated **GPI-PLD** activity present in the placenta in pre-eclampsia may be correctable by administration of **GPI-PLD** to the mother to correct the problems caused by abnormal or dysregulated **GPI-PLD**, e.g. to reduce the abnormal release and in situ prodn. of placental **IPGs** (inositol phosphoglycans) involved in the pathogenesis of pre-eclampsia. This can be achieved using exogenous **GPI-PLD** or a fragment thereof, e.g. an inactive **GPI-PLD** capable of competing with or displacing the abnormal or dysregulated **GPI-PLD**, e.g. from Apo-A1.

L7 ANSWER 2 OF 3 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001608363 MEDLINE
DOCUMENT NUMBER: 21539556 PubMed ID: 11683370
TITLE: Purification and characterization of insulin-mimetic inositol phosphoglycan-like molecules from grass pea (Lathyrus sativus) seeds.
AUTHOR: Paneda C; Villar A V; Alonso A; Goni F M; Varela F; Brodbeck U; Leon Y; Varela-Nieto I; Jones D R
CORPORATE SOURCE: Instituto de Investigaciones Biomedicas Alberto Sols (C.S.I.C.), Madrid, Spain.
SOURCE: MOLECULAR MEDICINE, (2001 Jul) 7 (7) 454-60.

Journal code: 9501023. ISSN: 1076-1551.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20011102
Last Updated on STN: 20020209
Entered Medline: 20020208

AB BACKGROUND: Signal transduction through the hydrolysis of glycosyl-phosphatidylinositol (GPI) leading to the release of the water-soluble inositol phosphoglycan (**IPG**) molecules has been demonstrated to be important for mediating some of the actions of insulin and insulin-like growth factor-I (IGF-I). MATERIALS AND METHODS: In the present study, GPI from grass pea (Lathyrus sativus) seeds has been purified and partially characterized on the basis of its chromatographic properties and its compositional analysis. RESULTS: The results indicate that it shows similarities to GPI previously isolated from other sources such as rat liver. **IPG** was generated from L. sativus seed GPI by hydrolysis with a GPI-specific phospholipase D (**GPI-PLD**). This **IPG** inhibited protein kinase A (PKA) in an in vitro assay, caused cell proliferation in explanted cochleovestibular ganglia (CVG), and decreased 8-Br-cAMP-induced phosphoenolpyruvate carboxykinase (PEPCK) mRNA expression in cultured hepatoma cells. CONCLUSIONS: Our data indicate that L. sativus seed **IPG** possess insulin-mimetic activities. This may explain why L. sativus seeds have been used in some traditional medicines to ameliorate diabetic symptoms.

L7 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:640696 CAPLUS
DOCUMENT NUMBER: 131:256346
TITLE: Antagonism of inositolphosphoglycan signaling in mast cells, basophils and eosinophils
INVENTOR(S): Rademacher, Thomas William; Whitby, Helen
PATENT ASSIGNEE(S): University College London, UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949855	A2	19991007	WO 1999-GB981	19990329
WO 9949855	A3	19991118		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319588	AA	19991007	CA 1999-2319588	19990329
AU 9931596	A1	19991018	AU 1999-31596	19990329
EP 1066043	A2	20010110	EP 1999-913481	19990329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-6645 A 19980327
WO 1999-GB981 W 19990329

AB The authors disclose that **inositolphosphoglycans** (**IPGs**) can be obtained from basophils, eosinophils and mast cells and that allergen stimulation of these cells results in **IPG** release. **IPGs**, acting as second messengers in non-allergen stimulated cells, induced histamine release or degranulation. Thus, **IPG** antagonists are envisioned for the treatment of conditions (esp. allergy and asthma) mediated by the release of **IPGs** from mast cells, basophils or eosinophils. Preferred **IPG** antagonists include anti-**IPG** antibodies, inhibitors of the enzyme **glycosylphosphatidylinositol phospholipase D**, and competitive antagonists.

=> dis his

(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD
L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCAN?))
L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7 3 DUP REM L6 (1 DUPLICATE REMOVED)

=> s l5 (10N) antibod?
L8 80 L5 (10N) ANTIBOD?

=> s l8 and pd<19980327
'19980327' NOT A VALID FIELD CODE
3 FILES SEARCHED...
L9 51 L8 AND PD<19980327

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10 25 DUP REM L9 (26 DUPLICATES REMOVED)

=> dis l10 1-25 ibib abs

L10 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:184077 CAPLUS
DOCUMENT NUMBER: 128:226252
TITLE: Materials and methods using P- and A-type inositolphosphoglycans and their antagonists for the diagnosis and treatment of diabetes and associated obesity
INVENTOR(S): Rademacher, Thomas William; McLean, Patricia
PATENT ASSIGNEE(S): Hoeft Rademacher Limited, UK; Rademacher, Thomas William; McLean, Patricia
SOURCE: PCT Int. Appl., 67 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9811435	A1	19980319	WO 1997-GB2440	19970911	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9741304	A1	19980402	AU 1997-41304	19970911	
AU 722425	B2	20000803			
EP 925503	A1	19990630	EP 1997-939083	19970911	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1234118	A	19991103	CN 1997-199097	19970911	
BR 9711753	A	20000118	BR 1997-11753	19970911	
JP 2001505658	T2	20010424	JP 1998-513366	19970911	

PRIORITY APPLN. INFO.: GB 1996-18934 A 19960911
WO 1997-GB2440 W 19970911

AB The diagnosis of diabetes based on the level or ratio of P- and A-type inositolphosphoglycans (IPGs) in a sample from a patient, and the use of P- and A-type IPGs or their antagonists in the treatment of diabetes, are disclosed. In particular, the invention provides treatment of IDDM or lean type II diabetes (NIDDM) with a mixt. of P- and A-type mediators, and treatment of obese type II diabetes (NIDDM) with a P-type mediator and/or an A-type antagonist.

L10 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180889 CAPLUS
DOCUMENT NUMBER: 128:240997
TITLE: Cyclitol containing carbohydrates from human tissue which regulate glycogen metabolism and their use in pharmaceuticals
INVENTOR(S): Rademacher, Thomas William; Caro, Hugo
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Caro, Hugo
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9811117	A1	19980319	WO 1997-GB2533	19970911	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9743101	A1	19980402	AU 1997-43101	19970911	
AU 713100	B2	19991125			
EP 925304	A1	19990630	EP 1997-919168	19970911	
EP 925304	B1	20000426			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 192160	E	20000515	AT 1997-919168	19970911	
ES 2147988	T3	20001001	ES 1997-919168	19970911	
JP 2001500859	T2	20010123	JP 1998-513410	19970911	
US 6271204	B1	20010807	US 1999-254748	19990614	

PRIORITY APPLN. INFO.: GB 1996-18929 A 19960911
WO 1997-GB2533 W 19970911

AB The application relates to the purifn. and characterization of a family of P-type inositolphosphoglycans (IPGs) from human liver and placenta. These substances are shown to have P-type biol. activity, e.g., activating pyruvate dehydrogenase (PDH) phosphatase. The characterization of the compds. demonstrates that they contain metal ions, in particular Mn2+ and/or Zn2+, and optionally phosphate. The compds. and their antagonists have uses as pharmaceuticals, e.g., for the treatment of diabetes, and in screening for synthetic analogs.

L10 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:180785 CAPLUS
DOCUMENT NUMBER: 128:226268
TITLE: P-type inositolphosphoglycans and antagonists thereof in diagnosis and treatment of pre-eclampsia and diabetes
INVENTOR(S): Rademacher, Thomas William; Mclean, Patricia
PATENT ASSIGNEE(S): Hoeft Rademacher Ltd., UK; Rademacher, Thomas William; Mclean, Patricia
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9810791	A1	19980319	WO 1997-GB2534	19970911	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9743102	A1	19980402	AU 1997-43102	19970911	
AU 715884	B2	20000210			
EP 939651	A1	19990908	EP 1997-919169	19970911	

EP 939651 B1 20000531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
CN 1235556 A 19991117 CN 1997-199318 19970911
BR 9711752 A 20000118 BR 1997-11752 19970911
AT 193452 E 20000615 AT 1997-919169 19970911
ES 2148967 T3 20001016 ES 1997-919169 19970911
JP 2001501598 T2 20010206 JP 1998-513411 19970911
PRIORITY APPLN. INFO.: GB 1996-18931 A 19960911
WO 1997-GB2534 W 19970911

AB The invention relates to materials and methods for the diagnosis and treatment of pre-eclampsia, and more particularly to the role of P-type inositolphosphoglycans (IPGs) in the occurrence of pre-eclampsia. Methods of diagnosing pre-eclampsia by detg. the level of P-type IPGs and uses of antagonists of P-type IPGs in the treatment of pre-eclampsia are disclosed, together with a method for screening for P-type IPG antagonists.

L10 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 1998:500068 CAPLUS
DOCUMENT NUMBER: 129:286317
TITLE: Induction of cell growth by insulin and insulin-like growth factor-I is associated with Jun expression in the otic vesicle
AUTHOR(S): Leon, Yolanda; Sanz, Carmen; Giraldez, Fernando; Varela-Nieto, Isabel
CORPORATE SOURCE: Instituto de Investigaciones Biomedicas, Consejo Superior de Investigaciones Cientificas (CSIC), Madrid, 28029, Spain
SOURCE: Journal of Comparative Neurology (1998), 398(3), 323-332
CODEN: JCNEAM; ISSN: 0021-9967
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The present report investigates the cellular mechanisms involved in the regulation of cell proliferation by insulin and insulin-like growth factor-I (IGF-I) in the developing inner ear of chick embryos. The results show that insulin and IGF-I stimulate cell proliferation in the otic vesicle. This effect is assocd. with the induction of the expression of the nuclear proto-oncogene c-jun. The temporal profile of Jun expression coincided with the proliferative period of growth of the otic vesicle. IGF-I promoted the hydrolysis of a membrane glycosyl-phosphatidylinositol, which was characterized as the endogenous precursor for inositol phosphoglycan (IPG). Both purified IPG and a synthetic analog, 6-O-(2-amino-2-deoxy-.alpha.-D-glucopyranosyl)-D-myo-inositol-1,2-cyclic phosphate (C3), were able to mimic the effects of IGF-I on Jun expression. Anti-**IPG antibodies** blocked the effects of IGF-I, which were rescued by the addn. of IPG or its analog. These results suggest that the sequence involving the hydrolysis of membrane glycolipids and the expression of c-jun and c-fos proto-oncogenes is part of the mechanism that activates cell division in response to insulin and IGF-I during early organogenesis of the avian inner ear. The implications of these observations for otic development and regeneration are briefly discussed.

L10 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1997:188451 CAPLUS
DOCUMENT NUMBER: 126:272579
TITLE: Inositol-phosphoglycan inhibits calcium oscillations in hepatocytes by reducing calcium entry
AUTHOR(S): Sanchez-Bueno, Antonio; Greenwood, Mark R.; Varela-Nieto, Isabel; Marrero, Isabel; Gil, Beatriz; Mato, Jose M.; Cobbold, Peter H.
CORPORATE SOURCE: Dep. Human Anatomy & Cell Biology, Univ. Liverpool, Liverpool, UK
SOURCE: Cell Calcium (1997), 21(2), 125-133
CODEN: CECADV; ISSN: 0143-4160
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inositol-phosphoglycan (IPG) is a putative mediator of insulin action that has been shown to affect numerous biochem. processes. IPG, prepd. from liver membranes, promptly inhibited phenylephrine- or vasopressin-induced [Ca2+]i oscillations when perfused over Fura-2-dextran injected rat hepatocytes. An **antibody** to **IPG** suppressed the inhibitory effect of insulin on the [Ca2+]i oscillations. Measurement of the rate of quench of cytoplasmic Fura-2 by extracellular Mn2+ showed that Ca2+ entry occurred continuously in the unstimulated cell and was not affected by phenylephrine or vasopressin. IPG, specifically, almost completely abolished the Mn2+ quench rate. Elevated extracellular [Ca2+] reversed the inhibitory effect of IPG on [Ca2+]i oscillations. We conclude that IPG inhibits the hepatocyte Ca2+ oscillator by reducing the continuous Ca2+ influx that is required to sustain oscillations in [Ca2+]i.

L10 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 2000:345870 CAPLUS
Correction of: 1997:525491
DOCUMENT NUMBER: 132:320044
Correction of: 127:232322
TITLE: HDL3 binds to glycosylphosphatidylinositol-anchored proteins to activate signalling pathways
AUTHOR(S): Nazih-Sanderson, Francoise; Lestavel, Sophie; Nion, Stephane; Rouy, Didier; Denefle, Patrice; Fruchart, Jean-Charles; Clavey, V.; Delbart, Christiane
CORPORATE SOURCE: Institut Pasteur, Lille, 59019, Fr.
SOURCE: Biochimica et Biophysica Acta (1997), 1358(1), 103-112
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have indicated that in HepG2 cells HDL3-signaling involves glycosylphosphatidylinositol (GPI) anchored proteins. HDL3-binding to HepG2 cells was found to be enhanced by cellular preincubation with PI-PLC inhibitors and sensitive to a cellular preincubation with exogenous PI-PLC, suggesting that HDL3 binds directly on GPI-anchored proteins to initiate signaling. Moreover HDL3-binding was found to be partly inhibited by antibodies against the HDL-binding protein (AbHBP). HDL3, when binding to HepG2 cells, promoted the release in the culture medium of a 110 kDa protein that binds AbHBP, while a cellular preincubation with **antibodies** against the inositol-phosphoglycan

(IPG) moiety of GPI-anchor (AbIPG), used to block lipolytic cleavage of the GPI-anchor, inhibits HDL3-induced release of the 110 kDa protein in the culture medium. In [3H]-PC prelabeled HepG2 cells, AbHBP were found to stimulate PC-hydrolysis and DAG generation within 5 min as did HDL3 stimulation. Cellular preincubation with AbIPG was found to inhibit only the HDL3-signal and not the AbHBP-signal, while a prior cellular pretreatment with PI-PLC from Bacillus cereus was found to inhibit the HDL3-and AbHBP-signal. Moreover cellular preincubation with AbHBP for 1 h at 37.degree.C was found to inhibit HDL3-signaling pathways. Our results suggest that in HepG2 cells a 110 kDa protein, which could be HBP, can be anchored to the membrane via GPI, and can function in HDL3-signaling pathways as binding sites. Previous studies have indicated that in HepG2 cells HDL3-signaling involves glycosylphosphatidylinositol (GPI) anchored proteins. HDL3-binding to HepG2 cells was found to be enhanced by cellular preincubation with PI-PLC inhibitors and sensitive to a cellular preincubation with exogenous PI-PLC, suggesting that HDL3 binds directly on GPI-anchored proteins to initiate signaling. Moreover HDL3-binding was found to be partly inhibited by antibodies against the HDL-binding protein (AbHBP). HDL3, when binding to HepG2 cells, promoted the release in the culture medium of a 110 kDa protein that binds AbHBP, while a cellular preincubation with **antibodies** against the inositol-phosphoglycan (**IPG**) moiety of GPI-anchor (AbIPG), used to block lipolytic cleavage of the GPI-anchor, inhibits HDL3-induced release of the 110 kDa protein in the culture medium. In [3H]-PC prelabeled HepG2 cells, AbHBP were found to stimulate PC-hydrolysis and DAG generation within 5 min as did HDL3 stimulation. Cellular preincubation with AbIPG was found to inhibit only the HDL3-signal and not the AbHBP-signal, while a prior cellular pretreatment with PI-PLC from Bacillus cereus was found to inhibit the HDL3-and AbHBP-signal. Moreover cellular preincubation with AbHBP for 1 h at 37.degree.C was found to inhibit HDL3-signaling pathways. Our results suggest that in HepG2 cells a 110 kDa protein, which could be HBP, can be anchored to the membrane via GPI, and can function in HDL3-signaling pathways as binding sites.

L10 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1997:256377 CAPLUS
DOCUMENT NUMBER: 126:328530
TITLE: HDL3-signaling in HepG2 cells involves glycosyl-phosphatidylinositol-anchored proteins
AUTHOR(S): Nazih-Sanderson, Francoise; Pinchon, Gaelle; Nion, Stephane; Fruchart, Jean-Charles; Delbart, Christiane
CORPORATE SOURCE: Unite INSERM 325, Institut Pasteur, 1 rue du Professeur Calmette BP 245-59019, Lille, Fr.
SOURCE: Biochimica et Biophysica Acta (1997), 1346(1), 45-60
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In [3H]phosphatidylcholine (PC) prelabeled HepG2 cells, HDL3 stimulates a biphasic increase in 1,2-diacylglycerol (DAG). The early phase is mediated in part by a phospholipase C which is inhibited by 10 .mu.M D 609, RHC-80267 or U-73122 and less by 100 .mu.M propranolol. A phospholipase D is more likely involved in the late phase, as the DAG peak lags behind phosphatidic acid rise and is blocked by 100 .mu.M propranolol. Cellular preincubation with 200 .mu.g/mL **antibodies** against the **inositolphosphoglycan** (**IPG**) moiety of the GPI-anchor (AbIPG), or depletion in GPI-anchored proteins by cellular pretreatment with 0.5 U/mL PI-PLC, 1 mM insulin and 2 HU/mL streptolysin-O, or depletion in membrane cholesterol content by filipin (5 .mu.g/mL), digitonin (5 .mu.g/mL) and cholesterol oxidase (0.5 U/mL) decreases the HDL3-signal, suggesting the involvement of a lipolytic cleavage of GPI-anchored proteins. Inhibition of proteases by 1 mM leupeptin/PMSF improves the response time to HDL3, with a DAG peak at 2-3 min. In the presence of protease-inhibitors, HDL3 releases in the culture medium several proteins with a residual IPG that binds AbIPG after SDS-PAGE anal. and immunoblotting. HDL3-signaling pathways comprise tyrosine kinases, as preincubation with 100 .mu.g/mL genistein or tyrphostin inhibits the HDL3-signal. HDL3 activates PC hydrolysis through a multistep pathway involving the cleavage of GPI-anchored proteins.

L10 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 5
ACCESSION NUMBER: 1995:716457 CAPLUS
DOCUMENT NUMBER: 123:103494
TITLE: Insulin-like growth factor-I regulates cell proliferation in the developing inner ear, activating glycosyl-phosphatidylinositol hydrolysis and fos expression
AUTHOR(S): Leon, Yoland; Vazquez, Esther; Sanz, Carmen; Vega, Jose A.; Mato, Jose M.; Giraldez, Fernando; Represa, Juan; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super Invest. Cient., Madrid, 28029, Spain
SOURCE: Endocrinology (1995), 136(8), 3494-503
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of insulin-like growth factors (IGF) was investigated during the early development of the inner ear. IGF-I stimulated growth of otic vesicles that were isolated and cultured in vitro. IGF-I induced DNA synthesis, increased cell no., and mitotic rate in a dose-dependent manner at concns. between 0.1-10 nM. IGF-I also induced growth but with a lower potency, whereas insulin had no effect. In the presence of IGF-I, otic vesicles developed from stage 18 to stage 21 in 24-h cultures, mimicking the normal mitotic pattern and morphogenesis in vivo. IGF-I also stimulated growth in the cochleo-vestibular ganglion. Binding of 125I-IGF-I to specific receptors occurred with high affinity. An autoradiog. study of sections from otic vesicles showed radiolabeled IGF-I in the epithelium. Immunoreactivity to IGF-I was detected in the otic vesicle and in the cochleo-vestibular ganglion. Intracellular signaling mechanisms of IGF were explored by studying the turnover of glycosylated phosphatidylinositols and the expression of Fos oncoprotein. IGF-I rapidly increased Fos levels in cultured otic vesicles. Furthermore, antisense oligonucleotides complementary to c-fos were able to inhibit IGF-I-induced growth. Both IGF-I-induced cell proliferation and Fos expression were blocked by an antiinositol phosphoglycan (.alpha.-**IPG**) **antibody**. This work suggests that IGF-I may be a candidate to regulate proliferative growth of the otic primordium during normal development and that this action requires the sequential modulation of glycosyl-phosphatidylinositol turnover and Fos expression.

L10 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6

ACCESSION NUMBER: 1995:727759 CAPLUS
DOCUMENT NUMBER: 123:133829
TITLE: Role of glycosyl-phosphatidylinositol hydrolysis as a mitogenic signal for epidermal growth factor
AUTHOR(S): Clemente, Rosa; Jones, David R.; Ochoa, Pilar; Romero, Guillermo; Mato, Jose M.; Varela-Nieto, Isabel
CORPORATE SOURCE: Consejo Superior de Investigaciones Cientificas (CSIC), Instituto de Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Cellular Signalling (1995), 7(4), 411-21
CODEN: CESIEY; ISSN: 0898-6568
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the role of the hydrolysis of glycosyl-phosphatidylinositol (GPI) as one of the signaling pathways elicited after interaction of epidermal growth factor (EGF) with its specific plasma membrane receptor (EGFR). Endogenous GPI was characterized in both NIH 3T3 mouse fibroblast cells and in EGFR-transfected NIH 3T3 cells (designated EGFR T17). GPI mols. isolated from both cell lines were identical and they incorporated radioactivity from both sugar and fatty acid substrates. Incubation of EGFR T17 cells with EGF, produced a rapid and transient hydrolysis of GPI. Max. hydrolysis occurred after a 1-min incubation with 50 nM EGF. No such effects of EGF were obsd. in the parental cell line. Both inositol phosphoglycan (IPG)-and EGF-induced cell proliferation was inhibited in the presence of an **IPG-antibody** to different extents.
The relation between GPI hydrolysis and the activity of the EGFR was studied using the tyrosine kinase inhibitors tyrphostin (RG50864) and genistein. These agents were able to significantly inhibit EGF-mediated cell proliferation, EGF-dependent hydrolysis of GPI and EGF-regulated autophosphorylation of the EGFR. It is concluded that GPI hydrolysis is one of the earliest intracellular events generated in response to EGF.

L10 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:647461 CAPLUS
DOCUMENT NUMBER: 123:29944
TITLE: Intracellular mediators of insulin-like growth factor I during otic vesicle development
AUTHOR(S): Leon, Yolanda; Sanz, Carmen; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Biochemical Society Transactions (1995), 23(2), 185S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors examd. the participation of the glycosylphosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of the proliferative effects of IGF-I in the developing otic vesicle and its relationship with Fos oncoprotein expression. IGF-I induced a fast and transient hydrolysis of GPI. The proliferative effects of IGF-I were coupled to GPI hydrolysis. The resulting IPG is a crucial step for the transduction of the mitogenic signal since anti-**IPG antibodies** decreased the effect on IF-I on otic vesicle growth in parallel with a decrease in Fos oncoprotein expression.

L10 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:647450 CAPLUS
DOCUMENT NUMBER: 123:26347
TITLE: Signalling at the epidermal growth factor receptor: role of glycosylphosphatidylinositol hydrolysis
AUTHOR(S): Jones, David R.; Clemente, Rosa; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Investigaciones Biomedicas, Madrid, 28029, Spain
SOURCE: Biochemical Society Transactions (1995), 23(2), 174S
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors investigated the involvement of glycosylphosphatidylinositol (GPI) hydrolysis during EGF-induced cell proliferation both in 3T3 cells and in 3T3 cells overexpressing the cloned human EGF receptor (EGFR T17 cells). The results showed that EGF modulated GPI turnover in an EGF receptor-dependent manner; EGF action was dose- and time-dependent; inositol phosphoglycan (**IPG**) specifically stimulated EGFR T17 cell proliferation; anti-**IPG antibodies** inhibited EGF-dependent cell proliferation; and tyrosine kinase inhibitors partially blocked GPI hydrolysis in parallel with the inhibition of both EGFR autophosphorylation and EGF-induced cell proliferation. proliferation. Thus, tyrosine kinase dependent-GPI hydrolysis may represent an early event in the transduction of the EGF signal in EGFR T17 cells.

L10 ANSWER 12 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 7
ACCESSION NUMBER: 93167402 EMBASE
DOCUMENT NUMBER: 1993167402
TITLE: IPG (inositolphosphate glycan) as a cellular signal for TGF-.beta.1 modulation of chondrocyte cell cycle.
AUTHOR: Vivien D.; Petitfrere E.; Martiny L.; Sartelet H.; Galera P.; Haye B.; Pujol J.-P.
CORPORATE SOURCE: Lab. Biochimie du Tissu Conjonctif, CJF INSERM 91-06, CHU Cote de Nacre,14033 Caen Cedex, France
SOURCE: Journal of Cellular Physiology, (1993) 155/3 (437-444).
ISSN: 0021-9541 CODEN: JCLLAX
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The knowledge of transforming growth factor (TGF)-.beta. receptors has greatly progressed in recent years. TGF-.beta. receptors type I and II have been implicated in the modulation of cell proliferation, whereas type III (betaglycan) may act as a component presenting TGF-.beta. to its signaling receptors. In addition, four other proteins that bind TGF-.beta.1 or TGF-.beta.2 have been recently identified in some cell lines, three being anchored to the membrane through a glycosylphosphatidylinositol (GPI). Despite this knowledge, the molecular mechanism of signal transduction through the TGF-.beta. receptors remain an enigma. TGF-.beta. family does not signal via any of the classical pathways. As GPI anchors of membrane proteins have been implicated in the

transduction of some hormonal effects, we investigated the putative role of GPI in signaling the TGF-.beta. effects on the proliferation of rabbit articular chondrocytes (RAC). We previously showed that TGF-.beta.1 increased DNA replication rate of RAC, with a recruitment of cells in G2/M followed by a subsequent mitosis wave. Here, we find that the factor causes specific GPI hydrolysis, with correlated increase of inositolphosphate glycan (**IPG**). This effect was specifically inhibited by **antibodies** that bind TGF-.beta.1. Using [3H]-inositol labeling and Triton X-114 extraction, we demonstrate that a hydrophobic material from the membrane is cleaved by treatment of cell cultures with phosphatidylinositol specific phospholipase C (PI-PLC) or by exposure to TGF-.beta., supporting that a PI-anchored molecule gives rise to IPG by TGF-.beta.-induced hydrolysis. The biological relevance of this hydrolysis was demonstrated by the enhancing effect of purified IPG on the DNA synthesis rate, which mimicked the TGF-.beta. action. These results demonstrate that IPG could be an early messenger in the cellular signaling that mediates the effect of TGF-.beta. on RAC growth.

L10 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1994:5158 CAPLUS
DOCUMENT NUMBER: 120:5158
TITLE: Brain-derived neurotrophic factor and neurotrophin-3 support the survival and neuritogenesis response of developing cochleovestibular ganglion neurons
AUTHOR(S): Avila, Matias A.; Varela-nieto, Isabel; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Van de Water, Thomas R.; Represa, Juan
CORPORATE SOURCE: Inst. Invest Biomed, Cons. Super. Invest. Cient., Madrid, 28029, Spain
SOURCE: Developmental Biology (Orlando, FL, United States) (**1993**), 159(1), 266-75
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) on the differentiation of avian cochleovestibular ganglion and their possible assocn. with the hydrolysis of glycosyl-phosphatidylinositol (GPI) were studied. BDNF and NT-3 (2 ng/mL) promoted neurite outgrowth in explants of both cochlear and vestibular ganglia. This effect on neuritogenesis was stage-dependent, reaching a max. at E7 for NT-3 and at E9 for BDNF. The magnitude of the response of the vestibular ganglion to BDNF was always smaller than that of the cochlear ganglion of an equiv. stage. BDNF and NT-3 stimulation of neuronal survival and neurite extension was also demonstrated in dissocd. neuronal cell cultures. The effect was concn.-dependent with satn. of the response occurring at 4 ng/mL for BDNF and at 2 ng/mL for NT-3, the half-maximal effect occurring at 2 and 1 ng/mL, resp., for the most sensitive stages of the chick cochlear ganglion. Inositol phosphoglycan (IPG) did not mimic the effects of BDNF or NT-3 on neuronal survival and neurite outgrowth, nor was it able to potentiate their responses. **Antibodies** raised against **IPG** did not block the effects of these neurotrophins. The results suggest that BDNF and NT-3 may act in cooperation to establish the innervation pattern of the inner ear. Unlike their early proliferative effects, neurotrophic effects are uncoupled from the GPI/IPG signal transduction system.

L10 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:618227 CAPLUS
DOCUMENT NUMBER: 119:218227
TITLE: Brain-derived neurotrophic factor and neurotropin-3 support the survival and neuritogenesis response of developing cochleovestibular ganglion neurons
AUTHOR(S): Avila, Matias A.; Varela-Nieto, Isabel; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Van De Water, Thomas R.; Represa, Juan
CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super. Invest. Cient., Madrid, 28029, Spain
SOURCE: Developmental Biology (Orlando, FL, United States) (**1993**), 159(2), 266-75
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) on the differentiation of avian cochleovestibular ganglion and their possible assocn. with the hydrolysis of glycosyl-phosphatidylinositol (GPI) were studied. BDNF and NT-3 (2 ng/mL) promoted neurite outgrowth in explants of both cochlear and vestibular ganglia. This effect on neuritogenesis was stage-dependent, reaching a max. at E7 for NT-3 and at E9 for BDNF. The magnitude of the response of the vestibular ganglion to BDNF was always smaller than that of the cochlear ganglion of an equiv. stage. BDNF and NT-3 stimulation of neuronal survival and neurite extension was also demonstrated in dissocd. neuronal cell cultures. The effects was concn.-dependent with satn. of the response occurring at 4 ng/mL for BDNF and at 2 ng/mL for NT-3, the half-maximal effect occurring at 2 and 1 ng/mL, resp., for the most sensitive stages of the chick cochlear ganglion. Inositol phosphoglycan (IPG) did not mimic the effects of BDNF or NT-3 on neuronal survival and neurite outgrowth, nor was it able to potentiate their responses. **Antibodies** raised against **IPG** did not block the effects of these neurotrophins. The results suggest that BDNF and NT-3 may act in cooperation to establish the innervation pattern of the inner ear. Unlike their early proliferative effects, neurotrophic effects are uncoupled from the GPI/IPG signal transduction system.

L10 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:5157 CAPLUS
DOCUMENT NUMBER: 120:5157
TITLE: Brain-derived neurotrophic factor and neurotrophin-3 induce cell proliferation in the cochleovestibular ganglion through a glycosyl-phosphatidylinositol signaling system
AUTHOR(S): Represa, Juan; Avila, Matias A.; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Verela-Nieto, Isabel
CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
SOURCE: Developmental Biology (Orlando, FL, United States) (**1993**), 159(1), 257-65
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have investigated the role of a brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3) in the regulation of cell proliferation in the early developing cochleovestibular ganglion (CVG).

Ganglia were isolated from 72-h chick embryos and cultured for 24 h. Both BDNF and NT-3 had a powerful mitogenic effect, at doses of 1-5 ng/mL, consistent with an involvement of the high-affinity receptor. Evidence for the participation of the glycosyl-phosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of proliferative effects of BDNF and NT-3 is presented. Both of these neurotrophins elicited a fast and transient hydrolysis of labeled GPI, approx. 60% in 30 s. The dose-response profile of GPI hydrolysis overlaps the neurotrophin-induced cell proliferation response profile. Anti-**IPG antibodies** were able to block the growth-promoting effects of BDNF and NT-3. Anti-**IPG antibodies** immunopptd. a CVG-endogenous **IPG**, induced upon BDNF treatment, which exhibited proliferative stimulating properties. Both BDNF and NT-3 are proposed as potential candidates for regulation of growth during CVG development, with this mitogenic effect being mediated by the GPI/IPG signaling system.

L10 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:618226 CAPLUS
DOCUMENT NUMBER: 119:218226
TITLE: Brain-derived neurotrophic factor and neurotrophin-3 induce cell proliferation in the cochleovestibular ganglion through a glycosyl-phosphatidylinositol signaling system
AUTHOR(S): Represa, Juan; Avila, Matias; Romero, Guillermo; Mato, Jose M.; Giraldez, Fernando; Varela-Nieto, Isabel
CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
SOURCE: Developmental Biology (Orlando, FL, United States) (**1993**), 159(2), 257-65
CODEN: DEBIAO; ISSN: 0012-1606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have investigated the role of brain-derived neurotrophic favor (BDNF) and neurotrophin-3 (NT-3) in the regulation of cell proliferation in the early developing cochleovestibular ganglion (CVG). Ganglia were isolated from 72-h chick embryos and cultured for 24 h. Both BDNF and NT-3 had a powerful mitogenic effect, at doses of 1-5 ng/mL, consistent with an involvement of the high-affinity receptor. Evidence for the participation of the glycosyl-phosphatidylinositol (GPI)/inositol phosphoglycan (IPG) signaling system in the mediation of proliferative effects of BDNF and NT-3 is presented. Both of these neurotrophins elicited a fast and transient hydrolysis of labeled GPI, approx. 60% in 30 s. The dose-response profile of GPI hydrolysis overlaps the neurotrophin-induced cell proliferation response profile. Anti-**IPG antibodies** were able to block the growth-promoting effects of BDNF and NT-3. Anti-**IPG antibodies** immunopptd. a CVG-endogenous **IPG**, induced upon BDNF treatment, which exhibited proliferative stimulating properties. Both BDNF and NT-3 are proposed as potential candidates for regulation of growth during CVG development, with this mitogenic effect being mediated by the GPI/IPG signaling system.

L10 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:1423 CAPLUS
DOCUMENT NUMBER: 120:1423
TITLE: Glycosyl-phosphatidylinositol: Role in neurotrophic factors signalling
AUTHOR(S): Avila, Matias A.; Leon, Yolanda; Gil, Beatriz; Varela-Nieto, Isabel
CORPORATE SOURCE: Inst. Invest. Biomed., Cons. Super. Invest. Cient., Madrid, 28029, Spain
SOURCE: NATO ASI Series, Series A: Life Sciences (**1993**), 246(New Developments in Lipid-Protein Interactions and Receptors Function), 103-13
CODEN: NALSDJ; ISSN: 0258-1213
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study provides further support for the involvement of the glycosyl-phosphatidylinositol/inositol-phosphoglycan (GPI/IPG) pathway in transducing the mitogenic effects of NGF on the early developing inner ear by showing: (1) the presence of endogenous GPI and IPG, the later with strong mitogenic activity, (2) the ability of NGF to stimulate GPI hydrolysis in parallel with its biol. activity, (3) the ability of anti-**IPG antibodies** to block the biol. effects on NGF.

L10 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1992:252962 CAPLUS
DOCUMENT NUMBER: 116:252962
TITLE: Role of the glycosylphosphatidylinositol/inositol phosphoglycan system in human fibroblast proliferation
AUTHOR(S): Vasta, Valeria; Bruni, Paola; Clemente, Rosa; Vannini, Fabio; Ochoa, Pilar; Romero, Guillermo; Farnararo, Marta; Varela-Nieto, Isabel
CORPORATE SOURCE: Dip. Sci. Biochim., Univ. Firenze, Florence, 50134, Italy
SOURCE: Experimental Cell Research (**1992**), 200(2), 439-43
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The involvement of the glycosylphosphatidylinositol/inositol phosphoglycan (gly-PtdIns/IPG) system in the stimulation of macromol. syntheses in human fibroblasts has been investigated. The study demonstrates that an insulin-sensitive gly-PtdIns/IPG system is present in human fibroblasts, that IPG can significantly stimulate DNA, RNA, and protein synthesis, and that the action of insulin on DNA synthesis as well as that of **IPG** can be significantly reduced by a specific anti-**IPG antibody**. These results strongly support the hypothesis that the gly-PtdIns/IPG system is involved in the signal transduction pathway leading to the stimulation of cell proliferation.

L10 ANSWER 19 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:410418 BIOSIS
DOCUMENT NUMBER: BA94:73618
TITLE: IMMOBILIZED PH GRADIENT ISOELECTRIC FOCUSING AND IMMUNOBLOTTING FOR INVESTIGATIONS OF ANTI-BORRELIA-BURGDORFERI IGG ANTIBODIES.
AUTHOR(S): CRUZ M; SIDEN A
CORPORATE SOURCE: DEP. NEUROL., HUDDINGE UNIV. HOSP., S-141 86 HUDDINGE, SWED.
SOURCE: ELECTROPHORESIS, (1992) 13 (4), 229-234.
CODEN: ELCTDN. ISSN: 0173-0835.
FILE SEGMENT: BA; OLD

LANGUAGE: English
AB Anti-Borrelia burgdorferi immunoglobulin G (IgG) responses in cerebrospinal fluid, serum, and joint fluid from Lyme disease patients were investigated by immobilized pH gradient (IPG) isoelectric focussing (IEF) in pH 4-10 and pH 4-7 gels. After focusing, the anti-B. burgdorferi antibodies were blotted by affinity-driven transfer to antigen-coated polyvinylidene difluoride membranes (immunoblot) and the IgG **antibodies** were immunoenzymatically stained. **IPG**-IEF gels gave an excellent resolution of IgG and the immunoblot proved advantageous for the detection of anti-B. burgdorferi IgG antibodies. These antibodies, as judged from the electromigration characteristics, were found to contain oligoclonal as well as polyclonal subpopulations. This latter group included IgG antibodies that were inadequately resolved when separated by conventional carrier ampholyte IEF.

L10 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1991:599685 CAPLUS
DOCUMENT NUMBER: 115:199685
TITLE: Glycosyl-phosphatidylinositol/inositol phosphoglycan: a signaling system for the low-affinity nerve growth factor receptor
AUTHOR(S): Represa, Juan; Avila, Matias A.; Miner, Cristina; Giraldez, Fernando; Romero, Guillermo; Clemente, Rosa; Mato, Jose M.; Varela-Nieto, Isabel
CORPORATE SOURCE: Fac. Med., Univ. Valladolid, Valladolid, 47005, Spain
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1991), 88(18), 8016-19
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nerve growth factor (NGF) exerts a variety of actions during embryonic development. At the early stages of inner ear development, NGF stimulates cell proliferation, an effect mediated through low-affinity receptors. The possibility that the glycosyl-phosphatidylinositol/inositol phosphoglycan (glycosyl-PtdIns/IPG) system is involved in transmitting this NGF signal was studied. Endogenous glycosyl-PtdIns was characterized in exts. of cochleovestibular ganglia (CVGs) that incorporated [3H]glucosamine, [3H]galactose, [3H]myristic acid, and [3H]palmitic acid. Incubation of CVG with NGF produced a rapid and transient hydrolysis of glycosyl-PtdIns. Hydrolysis was complete at 100 ng/mL, and the half-maximal effect occurred at 25 ng/mL, overlapping with the concn. dependence of the mitogenic effect of NGF. An IPG was isolated from embryonic exts. It had biol. effects similar to those reported for the insulin-induced IPG in other tissues. It exerted a powerful mitogenic effect on CVG, comparable to that of NGF. Both the **IPG**- and NGF-induced cell proliferation were blocked by anti-**IPG** **antibodies** that recognized the endogenous **IPG** on a silica plate immunoassay. These results show that CVG possesses a fully active glycosyl-PtdIns/IPG signal transduction system and that the proliferative effects assocd. with NGF binding to low-affinity receptors require IPG generation.

L10 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 12
ACCESSION NUMBER: 1991:22112 CAPLUS
DOCUMENT NUMBER: 114:22112
TITLE: Shifts of isoelectric points between cellular and secreted antibodies as revealed by isoelectric focusing and immobilized pH gradients
AUTHOR(S): Wenisch, Elisabeth; Reiter, Susanne; Hinger, Susanne; Steindl, Franz; Tauer, Christa; Jungbauer, Alois; Katinger, Hermann; Righetti, Pier Giorgio
CORPORATE SOURCE: Inst. Appl. Microbiol., Univ. Agric. For., Vienna, Austria
SOURCE: Electrophoresis (1990), 11(11), 966-9
CODEN: ELCTDN; ISSN: 0173-0835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Charge microheterogeneity of monoclonal antibodies, as revealed by isoelec. focusing in carrier ampholytes, has been known for a long time. Here in the case of monoclonals against the gp41 of the HIV-1 virus, this heterogeneity is already present within the cell sap of hybridoma cells during antibody synthesis. When the monoclonals are secreted extracellularly, the same pI spectrum is maintained, but there is a marked redistribution of the relative isoform abundance towards the lower pI components. This suggests in vivo processing of such forms, possibly via glycosylation or deamidation. The secreted **antibodies** are also analyzed by immobilized pH gradients (**IPG**), where they demonstrate an even more extensive heterogeneity, due to the marked increment in resolving power. Single bands are purified by preparative IPGs in a multicompartment electrolyzer and are shown to be stable with time. Thus, artifactual heterogeneity produced by the focusing technique is completely excluded and cellular processing is clearly established.

L10 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1990:135487 CAPLUS
DOCUMENT NUMBER: 112:135487
TITLE: Analytical isoelectric focusing with immobilized pH gradients of human apolipoprotein E from very low density lipoproteins and total plasma
AUTHOR(S): Mailly, France; Davignon, Jean; Nestruck, A. Christine
CORPORATE SOURCE: Hyperlipidemia Atherosclerosis Res. Group, Inst. Rech. Clin. Montreal, Montreal, PQ, H2W 1R7, Can.
SOURCE: J. Lipid Res. (1990), 31(1), 149-55
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method for anal. isoelec. focusing (IEF) of apolipoprotein E (apoE) in immobilized pH gradients (IPG) and immunodetection of the sepd. isoforms has been developed for use with either very-low-d. lipoproteins (VLDL) or whole plasma. Both VLDL and plasma were sequentially delipidated with 1,4-dioxane, acetone-ethanol, and ether. Neuraminidase treatment preceded the delipidation when required. Using preformed plates, pH 5.0-6.0 (LKB, Bromma) after rehydration with 6M urea and dextran T-10, the IPG focusing pattern of the common isoforms (E2, E3, E4) was found to be equiv. to conventional IEF with the added resoln. of the E4 disialo form. The use of self-poured narrower gradients permitted the further resoln. of the E4 monosialo form, a previously unrecognized heterogeneity of the E2, E3, and E4 monosialo isoforms and differentiation of the apoE2** mutant; all of these forms comigrate with the common isoproteins in conventional IEF. Finally, the conditions for **IPG** of whole plasma using apoE monoclonal **antibodies** and enzyme-conjugated anti-mouse IgG for detection were established. Thus, IPG focusing is shown to be a powerful

method for resoln. of the apoE sialoforms and apoE mutant forms. The method has important implications in accurate and diagnostic phenotyping. Moreover, it is a convenient method for phenotyping which requires only very small vols. of plasma.

L10 ANSWER 23 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 14
ACCESSION NUMBER: 87059320 EMBASE
DOCUMENT NUMBER: 1987059320
TITLE: A double-blind placebo-controlled trial of polymerized whole grass administered in an accelerated dosage schedule for immunotherapy of grass pollinosis.
AUTHOR: Grammer L.C.; Shaughnessy M.A.; Finkle S.M.; et al.
CORPORATE SOURCE: Section of Allergy-Immunology, Department of Medicine, Northwestern University Medical School, Chicago, IL 60611, United States
SOURCE: Journal of Allergy and Clinical Immunology, (1986) 78/6 (1180-1184).
CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
AB Forty-four patients were entered into a study of the efficacy and safety of individually polymerized grass (IPG) immunotherapy with an accelerated dosage schedule. Patients were paired on the basis of cutaneous end point titrations to timothy, orchard, and Bermuda grass-pollen extracts. In a double-blind manner, one patient in each pair was treated in nine weekly visits with 13 injections that totaled 24,000 PNU of each grass to which the patient had cutaneous reactivity. The other patient in each pair received caramelized glucose histamine placebo. Symptom and medication score sheets were completed by 33 patients each day of the grass season. Blocking **antibody** rose significantly in the **IPG** -treated group but was unchanged in the placebo-treated group. By Wilcoxon paired signed-rank test, the symptom medication scores in the IPG-treated group were significantly lower than those in the placebo-treated group. There were no systemic reactions and no clinically significant changes in routine laboratory tests in either group. In summation, this study demonstrates the safety, immunogenicity, and efficacy of IPG therapy in an accelerated dosage schedule for treatment of grass pollinosis.

L10 ANSWER 24 OF 25 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 15
ACCESSION NUMBER: 84030958 EMBASE
DOCUMENT NUMBER: 1984030958
TITLE: A double-blind histamine placebo-controlled trial of polymerized whole grass for immunotherapy of grass allergy.
AUTHOR: Grammer L.C.; Shaughnessy M.A.; Suszko I.M.; et al.
CORPORATE SOURCE: Section of Allergy-Immunology, Department of Medicine, Northwestern University Medical School, Chicago, IL 60611, United States
SOURCE: Journal of Allergy and Clinical Immunology, (1983) 72/5 I (448-453).
CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 038 Adverse Reactions Titles
037 Drug Literature Index
026 Immunology, Serology and Transplantation
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
LANGUAGE: English
AB Twenty-six patients were recruited for a study of the safety and efficacy of immunotherapy with IPG. They were randomly assigned to two groups based on skin test titrations to grass allergens. One group was treated in a double-blind fashion before the 1982 grass season with 12 weekly injections totaling approximately 48,000 PNU, and the other group was treated with 12 weekly injections of caramelized glucose histamine placebo. Daily symptom and medication score sheets were completed by all patients each day of the grass season. Blocking **antibody** rose ninefold in the **IPG** group ($p < 0.007$) but was unchanged in the placebo group. There was no significant change in IgE against rye grass group I in either the IPG or the placebo group. Symptom-score mean in the IPG group was 217 .+-. 71 (S.E.M.), statistically lower ($p < 0.02$) than the mean in the placebo group 496 .+-. 117 (S.E.M.). There were no systemic reactions and only minor local reactions. There was no change in routine laboratory tests in either group. Although two prior studies with grass allergen immunotherapy reported efficacy, these studies did not use symptom-score analysis. This is the first double-blind, histamine placebo-controlled study of grass immunotherapy that demonstrates efficacy by symptom-score index evaluation. IPG is a safe, clinically effective, and potentially cost-effective therapy for grass pollinosis.

L10 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:164188 CAPLUS
DOCUMENT NUMBER: 88:164188
TITLE: Pharmacological studies on an iron-poly(sorbitol-gluconic acid) complex for parenteral treatment of iron deficiency anemia
AUTHOR(S): Eriksson, Hans; Svard, Per Olov
CORPORATE SOURCE: Res. Dev. Lab., Astra Lakemedel AB, Sodertalje, Swed.
SOURCE: Scand. J. Haematol., Suppl. (1977), 32, 38-49
CODEN: SJHSBD; ISSN: 0080-6722
DOCUMENT TYPE: Journal
LANGUAGE: English
AB I.v. injection of the iron-poly(sorbitol-gluconic acid) complex (IPSG) to cats caused a transient decrease in mean arterial blood pressure and a temporary increase in central venous pressure, heart rate and femoral blood flow at large doses (cumulative doses up to 744 mg/kg). Tachyphylaxis developed upon repeated administration. A temporary redn. in the magnitude of the blood pressure responses to noradrenaline and isoprenaline was obtained after large doses of IPSG. The blood pressure effects of acetylcholine, histamine and bilateral carotid occlusion were not affected. No definite effects were seen on the EKGs. The transient cardiovascular effects were interpreted as being due to the presence of small amts. of Fe^{2+} in the prepn. IPSG did not affect blood coagulation or platelet aggregation. Immunogenicity studies in rabbits and **antibody** analyses of sera from patients treated with **IPGS** failed to demonstrate any effect of IPGS on the immune system.

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=> dis his

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     (FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1          550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2           47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3           28 DUP REM L2 (19 DUPLICATES REMOVED)
L4            1 S L3 AND GPI-PLD
L5         1504 S  (IPG OR (INOSITOLPHOSPHOGLYCAN?))
L6            4 S L5   (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7            3 DUP REM L6 (1 DUPLICATE REMOVED)
L8           80 S L5 (10N) ANTIBOD?
L9           51 S L8 AND PD<19980327
L10          25 DUP REM L9 (26 DUPLICATES REMOVED)

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))\
MISSING OPERATOR INOSITOL))\
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
L11       9525 (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))

=> s (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) antibod?
L12        122 (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?

=>  s l12 and PD<19980327
'19980327' NOT A VALID FIELD CODE
   3 FILES SEARCHED...
L13         67 L12 AND PD<19980327

=> dup rem  l13
PROCESSING COMPLETED FOR L13
L14          42 DUP REM L13 (25 DUPLICATES REMOVED)

=> s l14 (10N) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L59 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L61 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L63 (10A) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L65 (10A) ADMINIST?'
L15           0 L14 (10N) ADMINIST?

=> s l14 (P) administ?
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L68 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L70 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L72 (P) ADMINIST?'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L74 (P) ADMINIST?'
L16           0 L14 (P) ADMINIST?

=> dis l14 1-42 ibib abs

L14  ANSWER 1 OF 42  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        1998:180888  CAPLUS
DOCUMENT NUMBER:         128:242350
TITLE:                   A type A glycosylphosphatidylinositol second messenger
                         from human tissue involve in regulation of lipogenesis
INVENTOR(S):             Rademacher, Thomas William; Caro, Hugo
PATENT ASSIGNEE(S):      Hoeft Rademacher Ltd., UK; Rademacher, Thomas William;
                         Caro, Hugo
SOURCE:                  PCT Int. Appl., 62 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 9811116         A1   19980319       WO 1997-GB2444   19970911 <--
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,
             KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
             US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9741307         A1   19980402       AU 1997-41307    19970911
     AU 713103          B2   19991125
     EP 925305          A1   19990630       EP 1997-939087   19970911
     EP 925305          B1   20000426
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     AT 192161          E    20000515       AT 1997-939087   19970911
     ES 2147996         T3   20001001       ES 1997-939087   19970911
     JP 2001504450      T2   20010403       JP 1998-513368   19970911
     US 6303580         B1   20011016       US 1999-254797   19990604
     US 2001039027      A1   20011108       US 2001-775856   20010201
PRIORITY APPLN. INFO.:                    GB 1996-18930    A  19960911
                                          WO 1997-GB2444   W  19970911
                                          US 1999-254797   A3 19990604
AB   A family of A-type inositolphosphoglycans (IPGs) from human liver and
     placenta that appear to play a role in the regulation of lipogenesis are
     identified and characterized.  These substances have the biol. activity
     assocd. with A-type IPG fractions, namely regulating lipogenic activity
     and inhibiting cAMP dependent protein kinase.  The characterization of the
     compds. demonstrates that they contain metal ions, in particular Zn2+, and
     optionally phosphate.  The compds. and their antagonists have uses as
     pharmaceuticals, e.g. for the treatment of diabetes, and in screening for
     synthetic analogs.

L14  ANSWER 2 OF 42  CAPLUS  COPYRIGHT 2002 ACS        DUPLICATE 1
ACCESSION NUMBER:        1998:645582  CAPLUS
DOCUMENT NUMBER:         130:3032
TITLE:                   Antibody crosslinking of the
                         glycosylphosphatidylinositol-linked protein
```

CD59 on hematopoietic cells induces signaling pathways resembling activation by complement
AUTHOR(S): Murray, Elizabeth W.; Robbins, Stephen M.
CORPORATE SOURCE: Cancer Biology and Immunology Research Groups, Departments of Oncology and Biochemistry and Molecular Biology, University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Journal of Biological Chemistry (1998), 273(39), 25279-25284
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD59 is a glycosylphosphatidylinositol-anchored cell surface glycoprotein involved in protecting cells from host-mediated complement attack. Studies have shown that antibody crosslinking of CD59 induces a series of intracellular signaling events including the activation of protein-tyrosine kinases (PTK). To further characterize these events, antibodies and complement 8, one of the natural ligands of CD59, were used to activate CD59. Antibody-induced crosslinking of CD59 on the surface of THP-1 and U937 hematopoietic cell lines as well as exposure to complement 8 induces a rapid increase in the tyrosine phosphorylation of several proteins within the cell. Consistent with an early role for the Src family PTKs in these signaling events, we found that transient activation of Hck- and CD59-mediated signaling was abrogated in the presence of the Src family PTK-selective inhibitor PP1. Although the mol. mechanism by which CD59 communicates to Hck is unknown, cellular fractionation studies indicated that both CD59 and Hck are compartmentalized in plasma membrane microdomains. We also detected tyrosine phosphorylation of the adaptor proteins p120cbl and Shc, and the cytoplasmic nonreceptor tyrosine kinase Syk. The identification of CD59-mediated signaling events may help explain why paroxysmal nocturnal hemoglobinuria patients, who are deficient in glycosylphosphatidylinositol-linked proteins including CD59, are susceptible to proliferative disorders.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:130801 CAPLUS
DOCUMENT NUMBER: 128:256338
TITLE: Cell activation mediated by glycosylphosphatidylinositol-anchored or transmembrane forms of CD14
AUTHOR(S): Pugin, J.; Kravchenko, V. V.; Lee, J. -D.; Kline, L.; Ulevitch, R. J.; Tobias, P. S.
CORPORATE SOURCE: Division of Medical Intensive Care, University Hospital, Geneva, 1211/14, Switz.
SOURCE: Infection and Immunity (1998), 66(3), 1174-1180
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD14 is a glycosylphosphatidylinositol (GPI)-anchored membrane glycoprotein which functions as a receptor on myeloid cells for ligands derived from microbial pathogens such as lipopolysaccharide (LPS). We have studied the importance of the GPI tail of CD14 in signaling with the promonocytic cell line THP-1 expressing recombinant CD14 in a GPI-anchored form (THP1-wtCD14 cells) or in a transmembrane form (THP1-tmCD14). We found that, like other GPI-anchored mols., GPI-anchored CD14 was recovered mainly from a Triton X-100-insol. fraction, whereas transmembrane CD14 was fully sol. in Triton X-100. LPS induced cell activation of THP1-wtCD14 and of THP1-tmCD14 (protein tyrosine kinase phosphorylation, NF-.kappa.B activation, and cytokine prodn.) in a very similar manner. However, anti-CD14 antibody-induced crosslinking caused a rapid calcium mobilization signal only in GPI-anchored CD14 cells. Studies with pharmacol. inhibitors of intracellular signaling events implicate phospholipase C and protein tyrosine kinases in the genesis of this antibody-induced calcium signal. Our results suggest that GPI anchoring and CD14 targeting to glycolipid-rich membrane microdomains are not required for LPS-mediated myeloid cell activation. GPI anchoring may however be important for other signaling functions, such as those events reflected by antibody crosslinking.

L14 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:583862 CAPLUS
DOCUMENT NUMBER: 129:301394
TITLE: The glycosylphosphatidylinositol-anchored form and the transmembrane form of CD58 are released from the cell surface upon antibody binding
AUTHOR(S): Itzhaky, Dganit; Raz, Nava; Hollander, Nurit
CORPORATE SOURCE: Department Human Microbiology, Sackler School Medicine, Tel-Aviv University, Tel-Aviv, 69978, Israel
SOURCE: Cellular Immunology (1998), 187(2), 151-157
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The adhesion mol. CD58 is expressed on the cell surface in both a transmembrane form and a glycosylphosphatidylinositol (GPI)-anchored form. Here the authors report that CD58 is released from JY cells following crosslinking by immobilized anti-CD58 monoclonal antibodies. Antibodies to other cell surface proteins, as well as PMA and LPS, did not trigger CD58 release. The release resulted from membrane cleavage, since biotin-labeled CD58 was released from biotinylated cells, and down-modulation of CD58 surface expression accompanied accumulation of sol. CD58 in culture media. The authors have previously reported the isolation of JY variant cells, which lack expression of GPI-anchored proteins and thus express only the transmembrane form of CD58. Here they show that these variant cells release CD58 upon crosslinking, indicating that the transmembrane isoform is released, probably by proteolysis. Antibodies directed to the cytoplasmic domain of CD58, in contrast to antibodies against an extracellular epitope of CD58, did not react with released CD58, supporting a membrane cleavage mechanism. It is also shown that CD58, released from [3H]ethanolamine-labeled JY cells, contained ethanolamine. Thus, the GPI-anchored CD58 can be released in parallel to the transmembrane isoform and this release does not result from proteolytic cleavage, since cleavage by a protease would have removed the ethanolamine. Apparently, the 2 isoforms of CD58 are released upon antibody binding and their release is mediated by distinct mechanisms. (c) 1998 Academic Press.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:34080 CAPLUS
DOCUMENT NUMBER: 126:55943
TITLE: cysteine-rich glycosylphosphatidylinositol-anchored (CRG) protein gene marker for squamous cell carcinoma and bladder carcinoma as well as methods for diagnosis and treatment of these carcinomas
INVENTOR(S): Brakenhoff, Rudolf Henrikus; Van Dongen, Augustina Antonius Maria Sylvester
PATENT ASSIGNEE(S): Centocor B.V., Neth.; Brakenhoff, Rudolf, Henrikus; Van Dongen, Augustina, Antonius, Maria, Sylvester
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9635808	A1	19961114	WO 1995-NL168	19950510 <--
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9523758	A1	19961129	AU 1995-23758	19950510 <--
EP 828852	A1	19980318	EP 1995-916864	19950510 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				

PRIORITY APPLN. INFO.: WO 1995-NL168 19950510
AB The subject invention lies in the field of malignant diseases. More specifically the invention lies in the field of squamous cell carcinoma and bladder carcinoma. The invention covers diagnosis and treatment of such forms of carcinoma. In particular the invention includes the detn. of the presence and treatment of minimal residual disease, micrometastases or dissemination of such carcinoma types using nucleic acid hybridization or monoclonal antibody probes. The invention also includes gene therapy or vaccine development for treatment of carcinomas using cysteine-rich glycosylphosphatidylinositol-anchored protein (CRG protein) gene and expression vector constructs. CRG protein cDNA sequence is included, as well as characterization of CRG protein as the monoclonal antibody E48 antigen.

L14 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
ACCESSION NUMBER: 1996:355169 CAPLUS
TITLE: The use of monoclonal antibodies and flow cytometry in the diagnosis of paroxysmal nocturnal hemoglobinuria
AUTHOR(S): Hall, Sharon E.; Rosse, Wendell F.
CORPORATE SOURCE: Department of Medicine, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Blood (1996), 87(12), 5332-5340
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have characterized the erythrocytes, granulocytes, and platelets of 54 patients with paroxysmal nocturnal hemoglobinuria (PNH) with **antibodies** to **glycosylphosphatidylinositol**-anchored proteins (anti-CD55, anti-CD59, and anti-CD16) and flow cytometry to establish the usefulness of this technique in the diagnosis of this disorder. All patients demonstrated either completely (PNH III) or partially (PNH II) deficient red cells and granulocytes. Anti-CD59 best demonstrated PNH II red cells, which were present in 50% of the patients. The proportion of abnormal granulocytes was usually greater than the proportion of abnormal red cells; 37% of the patients had >80% abnormal granulocytes. Anti-CD55 did not delineate the erythrocyte populations as well as did anti-CD59. Either anti-CD55 or anti-CD59 could be used equally well to analyze granulocytes; anti-CD16 did not demonstrate cells of partial deficiency. Platelets could not be used for detailed anal. as the normal and abnormal populations were not well distinguished. Flow cytometry of erythrocytes using anti-CD59 or of granulocytes using either anti-CD55 or anti-CD59 provides the most accurate technique for the diagnosis of paroxysmal nocturnal hemoglobinuria; it is clearly more specific, more quant., and more sensitive than the tests for PNH that depend upon hemolysis by complement (the acidified serum lysis [Ham] test, the sucrose lysis test, and the complement lysis sensitivity [CLS] test).

L14 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:123084 CAPLUS
DOCUMENT NUMBER: 124:172196
TITLE: Glycosylphosphatidylinositol toxin of Plasmodium induces nitric oxide synthase expression in macrophages and vascular endothelial cells by a protein tyrosine kinase-dependent and protein kinase C-dependent signaling pathway
AUTHOR(S): Tachado, Souvenir D.; Gerold, Peter; McConville, Malcolm J.; Baldwin, Tracey; Quilici, Denis; Schwarz, Ralph T.; Schofield, Louis
CORPORATE SOURCE: Immunoparasitology Unit, Royal Melbourne Hosp., Victoria, 3050, Australia
SOURCE: Journal of Immunology (1996), 156(5), 1897-907
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, the authors demonstrate that glycosylphosphatidylinositol (GPI) is a major toxin of Plasmodium falciparum origin responsible for nitric oxide (NO) prodn. in host cells. Purified malarial GPI is sufficient to induce NO release in a time- and dose-dependent manner in macrophages and vascular endothelial cells, and regulates inducible NO synthase expression in macrophages. GPI-induced NO prodn. was blocked by the NO synthase-specific inhibitor L-N-monomethylarginine. GPI also synergizes with IFN-.gamma. in regulating NO prodn. The structurally related mols. dipalmitoylphosphatidylinositol and iM4 glycoinositolphospholipid from Leishmania mexicana had no such activity, and the latter antagonized IFN-.gamma.-induced NO output. GPI activates macrophages by initiating an early onset tyrosine kinase-mediated signaling process, similar to that induced by total parasite exts. The tyrosine kinase antagonists tyrphostin and genistein inhibited the release

of NO by parasite exts. and by GPI, alone or in combination with IFN-.gamma., demonstrating the involvement of one or more tyrosine kinases in the signaling cascade. GPI-induced NO release was also blocked by the protein kinase C inhibitor calphostin C, demonstrating a role for protein kinase C in GPI-mediated cell signaling, and by pyrrolidine dithiocarbamate, indicating the involvement of the NF-.kappa.B/c-rel family of transcription factors in cell activation. A neutralizing mAb to malarial GPI inhibited NO prodn. induced by GPI and total malarial parasite exts. in human vascular endothelial cells and murine macrophages, indicating that GPI is a necessary agent of parasite origin in parasite-induced NO output. Thus, in contrast to dipalmitoylphosphatidylinositol and glycoinositolphospholipids of Leishmania, malarial GPI initiates a protein tyrosine kinase- and protein kinase C-mediated signal transduction pathway, regulating inducible NO synthase expression with the participation of NF-.kappa.B/c-rel, which leads to macrophage and vascular endothelial cell activation and downstream prodn. of NO. These events may play a role in the etiol. of severe malaria.

L14 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
ACCESSION NUMBER: 1996:363203 CAPLUS
DOCUMENT NUMBER: 125:54187
TITLE: mCD24 expression in the developing mouse brain and in zones of secondary neurogenesis in the adult
AUTHOR(S): Calaora, V.; Chazal, G.; Nielsen, P. J.; Rougon, G.; Moreau, H.
CORPORATE SOURCE: CNRS, Univ. Aix-Marseille II, Marseille, Fr.
SOURCE: Neuroscience (Oxford) (1996), 73(2), 581-594
CODEN: NRSCDN; ISSN: 0306-4522
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interactions mediated by cell surface glycoproteins are considered to be crucial during the formation of the nervous system. Using a monoclonal **antibody** directed to mCD24, a **glycosylphosphatidylinositol** -anchored membrane glycoprotein, we have mapped its distribution throughout the mouse cerebral cortex during development nd in young adult. Before birth, mCD24 immunoreactivity was obsd. in the intermediate zone, the cortical plate and the marginal zone, whereas the ventricular zones were immunoneg. After birth, mCD24 expression declined rapidly in the cortex, except in the corpus callosum (and other commissures in the brain) where immunoreactivity was still found until P20. Furthermore, mCD24 expression was maintained in young adults (until P60, at least) in zones of secondary neurogenesis, such as the granule cells of the dentate gyrus, the subventricular zone lining the anterior part of the lateral ventricles and a zone of cells extending between the striatum and the corpus callosum to the center of the olfactory bulb. In this area mCD24 and polysialic acid neural cell adhesion mol. stainings were superimposed, and this corresponded to the pathway of migration of the olfactory immature neurons (subependymal layer). A layer of ciliated ependymal cells, lining all the ventricular walls, was also immunoreactive for mCD24. Thus, except for these epithelial-like cells, mCD24 was essentially found assocd. with differentiating postmitotic neurons. Its spatiotemporal expression, both during development and in the adult, is compatible with a role for this glycoprotein in cell surface recognition and in signalling events occurring during neuronal migration and axonal growth.

L14 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:165185 CAPLUS
DOCUMENT NUMBER: 124:229899
TITLE: Emergence of CD51-, glycosylphosphatidylinositol-anchor-deficient lymphocytes in rheumatoid arthritis patients following Campath-1H treatment
AUTHOR(S): Brett, Sara J.; Baxter, Gillian; Cooper, Helen; Rowan, Wendy; Regan, Tessa; Tite, John; Rapson, Nick
CORPORATE SOURCE: Molecular Immunology Group, Wellcome Research Laboratories, Kent, BR3 3BS, UK
SOURCE: International Immunology (1996), 8(3), 325-34
CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD52 is a glycosylphosphatidyl-inositol (GPI)-linked glycoprotein expressed at high levels on normal T and B lymphocytes and at lower levels on monocytes, while being absent on granulocytes and bone marrow stem cell precursors. The emergence of CD52- lymphocytes of both T and B cell lineages was obsd. in three out of 25 rheumatoid arthritis patients treated with the humanized antibody Campath-1H in phase II clin. trial. Whereas the majority of CD52- B cells had disappeared from the peripheral blood by 3 mo post-treatment, both CD52- CD4+ and CD8+ T cells persisted in the circulation for at least 20 mo. In the two patients that were tested, the GPI-anchored surface mols. CD55 and CD59 were also absent on the CD52- cells, although expression of other cell surface transmembrane proteins (CD3, CD4 and CD2) was unaffected. The CD52- cells maintained a stable phenotype in vitro despite repeated re-stimulation in culture. Both CD52- and CD52+ clones, established from one of the patients, responded to a similar extent to several T cell mitogens, as assessed by proliferation, suggesting that a general defect in expression of GPI-linked mols. does not impair T cell activation. These data show that an immune attack against a GPI-anchored surface mol. can result in the selection of a GPI-anchor-deficient cell population. Despite the persistence of CD52- T cells in the peripheral blood, no adverse reactions assocd. with the presence of these cells were noted in any of the patients; in fact they responded with longer remission times after Campath-1H treatment than the other patients in the trial.

L14 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4
ACCESSION NUMBER: 1996:691799 CAPLUS
DOCUMENT NUMBER: 126:30101
TITLE: Monoclonal antibody LR-1 recognizes murine heat-stable antigen, a marker of antigen-presenting cells and developing hematopoietic cells
AUTHOR(S): Hunt, David W. C.; Jiang, Hui-Jun; Granville, David J.; King, Diane E.; Levy, Julia G.
CORPORATE SOURCE: Department Microbiology and Immunology, University British Columbia, Vancouver, BC, Can.
SOURCE: International Archives of Allergy and Immunology (1996), 111(3), 218-228
CODEN: IAAIEG; ISSN: 1018-2438
PUBLISHER: Karger
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The rat monoclonal antibody LR-1 was initially described to be reactive with an antigen present on murine splenic B lymphocytes. However, flow-cytometric analyses of cells obtained from thymus, bone marrow, spleen, and lymph nodes showed that LR-1 stained approx. 95, 95, 60-70 and 20%, resp., of cells present within these tissues in normal DBA/2 mice. The marker recognized by LR-1 was present on peripheral erythrocytes and splenic dendritic cells, and activation with lipopolysaccharide A further increased expression of this antigen by splenic B cells. This particular tissue and cellular distribution was similar to that delineated with monoclonal antibodies reactive with heat-stable antigen (HSA). Dual labeling studies were conducted to compare the reactivity patterns of LR-1 and the HSA-reactive monoclonal antibody J11d and indicated that both antibodies recognized splenocytes bearing B cell (IgM) or erythroid (TER-119, CD71) but not T cell (CD4, CD8) markers. Splenocytes exposed to phosphoinositol-specific phospholipase C showed marked redn. in LR-1 binding, indicating that this **antibody** recognized a **glycosylphosphatidylinositol**-anchored cell surface protein, consistent with the known structure of HSA. Mixing of LR-1 with the HSA-specific antibodies J11d or M1/69 provided flow-cytometric profiles indistinguishable from those obtained with either antibody alone. However, LR-1 inhibited M1/69 binding to splenocytes by 83%, while J11d reduced M1/69 binding to these cells by only 18%. This finding suggested that LR-1 and M1/69 recognize identical splenic HSA epitopes, while LR-1 and J11d bind distinct antigenic determinants of spleen HSA. Western blot anal. of splenocyte, thymocyte, bone marrow cell and erythrocyte detergent exts. revealed that LR-1 reacted with glycoforms of HSA of known mol. wts. (30-55 kD). Thus, LR-1 recognizes HSA, the murine analog of human CD24, and will be a useful reagent with which to investigate the role of HSA in the immune response and hematopoiesis.

L14 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:486907 CAPLUS
DOCUMENT NUMBER: 125:140041
TITLE: Identification of the sheep homolog of the monocyte cell surface molecule CD14
AUTHOR(S): Gupta, V. K.; McConnell, I.; Dalziel, R. G.; Hopkins, J.
CORPORATE SOURCE: Department of Veterinary Pathology, University of Edinburgh, Summerhall, Edinburgh, EH9 1QH, UK
SOURCE: Veterinary Immunology and Immunopathology (1996), 51(1,2), 89-99
CODEN: VIIMDS; ISSN: 0165-2427
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An ovine monocyte/macrophage cell surface antigen was recognized by 3 mouse monoclonal antibodies (mAbs) VPM65, VPM66, and VPM67. These mAbs also reacted with bovine cells. The **antibodies** immunopptd. a single, **glycosylphosphatidylinositol**-linked polypeptide of mol. wt. (Mr) 55,000 which, when deglycosylated, was reduced to Mr 53,000. They reacted strongly with peripheral blood monocytes, alveolar macrophages and peripheral blood granulocytes, and weakly with afferent lymph dendritic cells. They also reacted with macrophages in many different tissues but were non-reactive with lymphocytes. Competitive flow cytometry shows that these 3 mAbs recognize the same or a closely related epitope of a single antigen. An antigen-specific capture ELISA using the anti-human CD14 mAb (TUEK4) revealed that all 4 mAbs assoc. with the same antigen. Thus, the mAbs react with the ovine homolog of the lipopolysaccharide (LPS)-LPS binding protein receptor, CD14.

L14 ANSWER 12 OF 42 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 5
ACCESSION NUMBER: 95265248 EMBASE
DOCUMENT NUMBER: 1995265248
TITLE: Identification and characterization of a novel protein (p137) which transcytoses bidirectionally in Caco-2 cells.
AUTHOR: Ellis J.A.; Luzio J.P.
CORPORATE SOURCE: Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, Hills Road,Cambridge CB2 2QR, United Kingdom
SOURCE: Journal of Biological Chemistry, (1995) 270/35 (20717-20723).
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Antisera raised against detergent-extracted membrane fractions from the human intestinal epithelial cell line Caco-2 were used to screen a human colon cDNA library in a bacteriophage expression vector. This led to the identification, molecular cloning, and sequencing of a novel plasma membrane protein (p137) which was present in approximately equal amounts on the basolateral and apical surfaces of the cell. The pattern of extraction of p137 from membranes by Triton X-114 and its release from membranes after incubation with phosphatidylinositol-specific phospholipase C were consistent with it being a **glycosylphosphatidylinositol**-anchored membrane protein. Using **antibodies** raised against bacterial fusion proteins, it was shown that p137 was present on the cell surface as a reducible homodimer of 137 kDa subunits. There was constitutive release of p137 into the culture medium as a non- reducible 280-kDa entity. Pulse-chase experiments showed that newly synthesized p137 appeared at the basolateral side of a Caco-2 cell layer before appearing at the apical domain. Domain-specific surface biotinylation of Caco-2 cells at 4 .degree.C, followed by chasing at 37 .degree.C, demonstrated that p137 is capable of transcytosing in both directions across Caco-2 cells. The unusual plasma membrane domain distribution of this glycosylphosphatidylinositol-linked protein and its transcytosis characteristics demonstrate the existence of a previously uncharacterized apical to basolateral transcytotic pathway in Caco-2 cells.

L14 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1995:805891 CAPLUS
DOCUMENT NUMBER: 123:224310
TITLE: De novo formation of caveolae in lymphocytes by expression of VIP21-caveolin
AUTHOR(S): Fra, Anna M.; Williamson, Edward; Simons, Kai; Parton, Robert G.
CORPORATE SOURCE: European Mol. Biol. Lab., Heidelberg, Germany
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1995), 92(19), 8655-9
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Caveolae are plasma membrane invaginations, which have been implicated in endothelial transcytosis, endocytosis, potocytosis, and signal transduction. In addn. to their well-defined morphol., caveolae are characterized by the presence of an integral membrane protein termed VIP21-caveolin. The authors have recently obsd. that lymphocytes have no detectable VIP21-caveolin and lack plasma membrane invaginations resembling caveolae. Here the authors transiently express VIP21-caveolin in a lymphocyte cell line using the Semliki Forest virus expression system and show de novo formation of plasma membrane invaginations contg. VIP21-caveolin. These invaginations appear homogeneous in size and morphol. indistinguishable from caveolae of nonlymphoid cells. Moreover, the **glycosylphosphatidylinositol**-anchored protein Thy1, patched by **antibodies**, redistributes to the newly formed caveolae. The results show that VIP21-caveolin is a key structural component required for caveolar biogenesis.

L14 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:444475 CAPLUS
DOCUMENT NUMBER: 122:237244
TITLE: Primary structures of CD52
AUTHOR(S): Treumann, Achim; Lifely, M. Robert; Schneider, Pascal; Ferguson, Michael A. J.
CORPORATE SOURCE: Dep. Biochem., Univ. Dundee, Dundee, DD1 4HN, UK
SOURCE: Journal of Biological Chemistry (1995), 270(11), 6088-99
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The CD52 antigen was extd. from human spleens with org. solvents and purified by immunoaffinity and reverse-phase chromatog. The latter step resolved two CD52 species, called CD52-I and CD52-II. Both species were found to contain similar N-linked oligosaccharides and glycosylphosphatidylinositol (GPI) anchor glycans. The N-linked oligosaccharides were characterized by methylation linkage anal. and, following exhaustive neuraminidase and endo-.beta.-galactosidase digestion, by the reagent array anal. method. The results showed that the single CD52 N-glycosylation site is occupied by large sialylated, polylactosamine-contg., core-fucosylated tetraan-tennary oligosaccharides. The locations of the phosphoryl substituents on the GPI anchor glycan were detd. using a new and sensitive method based upon partial acid hydrolysis of the GPI glycan. The difference between CD52-I and CD52-II was in the phosphatidylinositol (PI) moieties of the GPI anchors. The phosphatidylinositol-specific phospholipase C-sensitive CD52-I contained exclusively distearoyl-PI, while the PI-phospholipase C-resistant CD52-II contained predominantly a palmitoylated stearoyl-arachidonoyl-PI, as judged by electrospray ionization mass spectrometry. Tandem mass spectrometric studies indicated that the palmitoyl residue of the CD52-II anchor is attached to the 2-position of the myo-inositol ring. Both the CD52-I and CD52-II PI structures are unusual for GPI anchors and the possible significance of this is discussed. The alkali-lability of the CD52 epitope recognized by the Campath-1H monoclonal antibody was studied. The data suggest that the alkali-labile hydroxyester-linked fatty acids of the GPI anchor are necessary for antibody binding.

L14 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:47622 CAPLUS
DOCUMENT NUMBER: 126:102866
TITLE: Identification of Workshop Endothelial Section mAb that recognize novel glycosyl phosphatidylinositol-anchored antigens
AUTHOR(S): Klickstein, Lloyd B.; York, Michael R.; Luther, Ed; Springer, Timothy A.
CORPORATE SOURCE: UK
SOURCE: Leucocyte Typing V: White Cell Differentiation Antigens, Proceedings of the International Workshop and Conference, 5th, Boston, Nov. 3-7, 1993 (**1995**), Meeting Date 1993, Volume 2, 1850-1852. Editor(s): Schlossman, Stuart F. Oxford University Press: Oxford, UK.
CODEN: 63WDAC
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The glycosylphosphatidylinositol anchor is a post-translational modification of newly synthesized proteins in which the polypeptide chain is cleaved at a signal sequence near the C-terminal end of the protein and a GPI moiety is transferred to the new C-terminal residue. Here, to identify monoclonal antibodies that recognize novel GPI-anchored antigens, human umbilical cord vein endothelial cells (HUVEC), with and without phosphatidylinositol-specific phospholipase C treatment, were analyzed by indirect immunofluorescence and flow cytometry.

L14 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:47459 CAPLUS
DOCUMENT NUMBER: 126:116717
TITLE: Identification of novel GPI-anchored antigens by analysis of GPI-anchor-deficient cells with mAb in the Blind Panel
AUTHOR(S): Klickstein, Lloyd B.; York, Michael R.; Luther, Ed; Springer, Timothy A.
CORPORATE SOURCE: UK
SOURCE: Leucocyte Typing V: White Cell Differentiation Antigens, Proceedings of the International Workshop and Conference, 5th, Boston, Nov. 3-7, 1993 (**1995**), Meeting Date 1993, Volume 2, 1478-1481. Editor(s): Schlossman, Stuart F. Oxford University Press: Oxford, UK.
CODEN: 63WDAC
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Studies with various cell lines, GPI-anchor-deficient cell lines, phospholipase C-treated cells, and monoclonal antibodies from the Fifth International Workshop on Human Leukocyte Antigens indicated that CD93, CD58, CDw108, CDw109, CDw75, and CDw76 are GPI anchored antigens. Antigens A049 (3F4), T010 (4dD8), and E057 (C4A9.2.3) also appear to be GPI anchored.

L14 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:47453 CAPLUS

DOCUMENT NUMBER: 126:102832
TITLE: Adhesion structure subpanel 1, E rosetting/GPI anchor: CD2, CD48, CD55, CD58, CD59, CD99, and CDw108
AUTHOR(S): Klickstein, Lloyd B.; Springer, Timothy A.
CORPORATE SOURCE: UK
SOURCE: Leucocyte Typing V: White Cell Differentiation Antigens, Proceedings of the International Workshop and Conference, 5th, Boston, Nov. 3-7, 1993 (**1995**), Meeting Date 1993, Volume 2, 1468-1471. Editor(s): Schlossman, Stuart F. Oxford University Press: Oxford, UK.
CODEN: 63WDAC
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors report cluster anal. and isotype for mouse and rat monoclonal antibodies to GPI-anchored surface antigens mediating adhesion. In addn., the authors examd. the effect of theses antibodies on PBMC proliferation.

L14 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 7
ACCESSION NUMBER: 1995:684499 CAPLUS
DOCUMENT NUMBER: 123:225436
TITLE: Investigations using a novel monoclonal **antibody** to the **glycosylphosphatidylinositol**-anchored protein that carries Gregory, Holley, and Dombrock blood group antigens
AUTHOR(S): Rao, N.; Udani, M.; Nelson, J.; Reid, M. E.; Telen, M. J.
CORPORATE SOURCE: Medical Center, Duke University, Durham, NC, USA
SOURCE: Transfusion (Bethesda, Maryland) (**1995**), 35(6), 459-64
CODEN: TRANAT; ISSN: 0041-1132
PUBLISHER: American Association of Blood Banks
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The high-frequency Hy and Gya antigens have been shown to reside on the same protein. Gy(a-) Hy-neg. red cells are also Do(a-b-). A mouse monoclonal antibody, 5B10, was produced with specificity related to the human Gregory, Holley, and Dombrock blood group antigens. The antibody reacted in direct hemagglutination assays, and its specificity was investigated by RIA, inhibition assay, and Western blotting. The 5B10 antibody failed to bind to abnormal paroxysmal nocturnal hemoglobinuria red cells and human erythroleukemia cell line K562, but it was weakly reactive with HEL cells. Red cells, but not other circulating hematopoietic cells, express the 5B10 antigen. The 5B10 antibody had a specificity similar but not identical to that of Gya. Gy(a-) Hy-neg. red cells reacted extremely weakly with 5B10 antibody, but Gy(a-) Hy-neg. red cells treated with a variety of proteases bound 5B10 antibody strongly. This suggests that these cells express a variant form of the protein recognized by 5B10. Identification of a monoclonal **antibody** to this **glycosylphosphatidylinositol**-linked protein opens a new avenue for investigation of the biochem., genetics, and function of the glycosylphosphatidylinositol-linked protein that bears the Gya, Hy, and Do antigens.

L14 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:523941 CAPLUS
DOCUMENT NUMBER: 123:77430
TITLE: Schistosoma mansoni: molecular cloning and sequencing of the 200-kDa chemotherapeutic target antigen
AUTHOR(S): Hall, Traci M. Tanaka; Joseph, Gerald T.; Strand, Mette
CORPORATE SOURCE: School of Medicine, Johns Hopkins University, Baltimore, MD, 21205, USA
SOURCE: Experimental Parasitology (**1995**), 80(2), 242-9
CODEN: EXPAAA; ISSN: 0014-4894
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Praziquantel is the drug of choice for human schistosomiasis. The efficacy of this drug is impaired in immune-deficient mice. However, transfer to B cell-depleted mice of a monoclonal antibody that recognizes a 200-kDa GPI-anchored glycoprotein of S. mansoni restores the effectiveness of praziquantel. In order to characterize this target antigen, we have isolated and sequenced cDNA clones encoding the 200-kDa protein. Three overlapping cDNA clones contained the complete nucleotide sequence. The sequences of five tryptic peptides from the native 200-kDa protein could be matched with regions in the amino acid sequence deduced from the nucleotide sequence of the isolated clones. This deduced amino acid sequence differed from sequences available in six databases. Praziquantel exposes epitopes on the worm surface that are normally not exposed, and we have shown by immunofluorescent staining that the fusion protein encoded by one of our cDNA clones expresses epitopes that are exposed on the surface of praziquantel-treated worms.

L14 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:406856 CAPLUS
DOCUMENT NUMBER: 121:6856
TITLE: An epitope on carcinoembryonic antigen defined by the clinically relevant antibody PR1A3
AUTHOR(S): Durbin, Helga; Young, Susan; Stewart, Lorna M.; Wrba, Fritz; Rowan, Andrew J.; Snary, David; Bodmer, Walter F.
CORPORATE SOURCE: Cancer Genet. Lab., Imp. Cancer Res. Fund, London, WC2A 3PX, UK
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (**1994**), 91(10), 4313-17
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The monoclonal antibody PR1A3 has been used successfully for in vivo imaging of colorectal cancers, and several properties assocd. with this antibody, including minimal reactions of the antibody with circulating antigen in patients' sera, differentiate it from anti-carcinoembryonic antigen (CEA) antibodies used in similar studies. However, the antigen bound by PR1A3 was identified as CEA by anal. of somatic cell hybrids and by antigen expression from yeast artificial chromosomes, cosmids, and cDNA clones. The mol. wt., presence of a glycosylphosphatidylinositol anchor, elevation of surface expression of .gamma.-interferon, and N-terminal amino acid sequence all confirmed the antigen identification as CEA. A series of biliary glycoprotein-CEA hybrid proteins was produced which demonstrated that the epitope bound by the antibody was at the site of

membrane attachment and involved parts of the glycosylphosphatidylinositol anchor and the B3 domain of CEA to form a conformational epitope. Access to this epitope, although possible when the antigen was on the cell surface, appeared to be blocked when CEA was released from the cell. The nature and location of the epitope on CEA are proposed to be responsible for the unique properties of the antibody.

L14 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:242358 CAPLUS
DOCUMENT NUMBER: 122:7931
TITLE: Recombinant glycosylphosphatidylinositol-anchored proteins are not associated with protein kinases in transfected thymoma cells
AUTHOR(S): Clissold, Patricia M.
CORPORATE SOURCE: Molecular Immunopathology Unit, MRC Centre, Cambridge, C82, 2QH, UK
SOURCE: Biochemical Journal (1994), 304(3), 853-9
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The crosslinking by **antibody** of some **glycosylphosphatidylinositol** (GPI)-anchored proteins on the plasma membrane of T cells leads to cell activation. Phosphorylation of proteins on tyrosine residues has a central role in the control of T cell activation, and non-receptor protein tyrosine kinases can be copptd. with immune complexes of GPI-anchored proteins in T cell lysates. To investigate the nature of this interaction, two recombinant GPI-anchored proteins were constructed (using the GPI signal sequence from Thy-1), and their assocns. with protein tyrosine kinases in stable transfectants of a mouse thymoma have been investigated. One recombinant GPI protein is the extracellular domain of the human complement receptor-1, normally an integral membrane protein, and the other is the secreted protein, human tissue inhibitor of human metalloproteinases. The latter protein should be foreign to the cell surface and yet has been expressed as a GPI-anchored protein at levels equiv. to the highly expressed antigens Thy-1 and Ly6 A2 on mouse thymoma cells. Neither of the two recombinant proteins, when immunopptd. from NP-40 lysates of transfected cells, were assocd. with protein tyrosine kinases in contrast with the natural endogenous GPI-anchored proteins Thy-1 and Ly6.A2 in non-transfected parental cells. Moreover, high expression of foreign recombinant GPI protein appears to interfere with the assocn. of the natural GPI proteins with protein tyrosine kinases.

L14 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:242361 CAPLUS
DOCUMENT NUMBER: 122:7553
TITLE: Lytic anti-.alpha.-galactosyl antibodies from patients with chronic Chagas' disease, recognize novel O-linked oligosaccharides on mucin-like glycosyl-phosphatidylinositol-anchored glycoproteins of Trypanosoma cruzi
AUTHOR(S): Almeida, Igor C.; Ferguson, Michael A.; Schenkman, Sergio; Travassos, Luiz R.
CORPORATE SOURCE: Disciplina de Biol. Celular, Esc. Paulista de Medicina, Sao Paulo, SP 04023-062, Brazil
SOURCE: Biochemical Journal (1994), 304(3), 793-802
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sera of patients with chronic Chagas' disease (American trypanosomiasis) contain elevated levels of anti-.alpha.-galactosyl antibodies that are lytic to Trypanosoma cruzi. The T. cruzi trypomastigote F2/3 antigen complex recognized by these antibodies runs as a broad smear on SDS-PAGE. Treatment of T. cruzi trypomastigote cells with bacterial phosphatidylinositol-specific phospholipase C (PI-PLC) abolished most of their reactivity to chagasic anti-.alpha.-galactosyl antibodies (anti-Gal). The F2/3 antigen complex, purified by solvent extn. and hydrophobic-interaction chromatog., contained 60% carbohydrate by wt. and substantial amts. of Thr, Ser, Glx, Asx, Gly, Ala and Pro, but relatively few hydrophobic amino acids. The presence of myo-inositol, ethanolamine and 1-O-hexadecylglycerol suggested the presence of glycosyl-phosphatidylinositol membrane anchors. This was confirmed by PI-PLC treatment, which rendered the F2/3 mols. hydrophilic and reactive to anti-(cross-reaching determinant) antibodies. The majority of the GlcNAc content of the F2/3 antigens was found at the reducing termini of oligosaccharides in O-glycosidic linkage to Thr residues. These O-linked oligosaccharides could be released by .beta.-elimination and by mild hydrazinolysis. The smallest released oligosaccharitol that was reactive with the chagasic anti-Gal was Gal.alpha.1-3Gal.beta.1-4GlcNAcol (where GlcNAcol is N-acetylglucosaminitol). Several other Gal-contg. oligosaccharitols were obsd., most of which were branched and contained 4,6-di-O-substituted GlcNAcol at their reducing termini. About half of the total released oligosaccharitols could bind to immobilized chagasic anti-Gal, but none of the bound to the anti-Gal isolated from normal human sera. These data suggest that the specificities of the chagasic anti-Gal are quite different from the natural anti-Gal isolated from normal human sera. Therefore, these novel T. cruzi O-linked oligosaccharides are highly immunogenic under the conditions of natural infection and are the targets for lytic chagasic anti-Gal.

L14 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1994:103099 CAPLUS
DOCUMENT NUMBER: 120:103099
TITLE: Expression and secretion of glycosylphosphatidylinositol-specific phospholipase D by myeloid cell lines
AUTHOR(S): Xie, Mingsheng; Low, Martin G.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Biochemical Journal (1994), 297(3), 547-54
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB All the myeloid cell lines tested, including K562 (multipotential blast), KG-1 (human myeloblast), HL-60, NB4, PLB-985 (human promyelocyte), U937 (human promonocyte), THP-1 (human monocyte) and J774, RAW264.7 (mouse monocyte/macrophage), contained glycosylphosphatidylinositol (GPI)-degrading activity. TLC anal. of reaction products confirmed the activity as a phospholipase D (PLD). These cells also exhibited pos. immunofluorescent staining with an anti-**GPI-PLD** monoclonal **antibody**. The expression of GPI-PLD activity was not

substantially reduced when the cells were cultured in either serum-free medium or GPI-PLD-depleted regular medium. Both granulocytic and monocytic differentiation of myelomonoblastic lines (e.g. HL-60) induced by DMSO or phorbol diester, resp., was accompanied by a 2-3-fold increase in GPI-PLD activity. J774 and HL-60 cells secreted GPI-PLD into the medium constitutively. Taken together, these data suggest that myeloid cells are a potential contributor to the circulating GPI-PLD pool. As leukocytes express many important GPI-anchored surface antigens, these cells may prove to be valuable model system for studying the physiol. functions of GPI-PLD.

L14 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:320921 CAPLUS
DOCUMENT NUMBER: 120:320921
TITLE: GPI-anchored glycoconjugates from Trypanosoma cruzi trypomastigotes are recognized by lytic anti-.alpha.-galactosyl antibodies isolated from patients with chronic Chagas' disease
AUTHOR(S): Almeida, I.C.; Ferguson, M.A.J.; Schenkman, S.; Travassos, L.R.
CORPORATE SOURCE: Discip. de Biol. Cel., Esc. Paul. de Med., Sao Paulo, 04023-062, Brazil
SOURCE: Brazilian Journal of Medical and Biological Research (**1994**), 27(2), 443-7
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The target mols. on the cell surface of Trypanosoma cruzi trypomastigotes reacting with lytic anti-.alpha.-galactosyl antibodies from chronic patients with Chagas' disease (Ch anti-Gal) have been purified by solvent extn. and identified as glycoconjugates migrating in the 74-96-kDa range (F2 antigen) and in the 120-200-kDa range (F3 antigen) on SDS-PAGE. The F3 antigen was tested for binding to Ch and normal human serum (NHS) anti-Gal and to MoAb 3C9. The authors obsd. that Ch anti-Gal and MoAb 3C9, but not NHS anti-Gal, bind strongly to the trypomastigote glycoconjugates. These antibodies, however, did not compete with each other for binding to F3 mols., indicating that they are recognizing different epitopes. Binding of Ch anti-Gal to F3 antigen is abolished by treatment of these mols. with .alpha.- but not .beta.-galactosidase. Binding of 3C9 MoAb is abolished by treatment of F3 with sialidase. F2/F3 antigens absorbed Ch anti-Gal as well as lytic antibodies from total chagasic sera. These antigens also specifically discriminate between the serum reactivity of patients with active Chagas' disease and those of sera from cured patients, drug-treated patients with dissocd. serol. (pos. conventional serol., neg. trypanolytic activity), healthy individuals, and patients with several other infectious diseases. The authors also obsd. that F2/F3 antigens are anchored to the parasite membrane via glycosylphosphatidylinositol (GPI). The .alpha.-galactosyl epitopes recognized by Ch anti-Gal are present in a series of O-linked oligosaccharide chains in the mucin-like glycoprotein component of the complex.

L14 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:320799 CAPLUS
DOCUMENT NUMBER: 120:320799
TITLE: Early molecular signals induced by antibodies to GPI-anchored proteins
AUTHOR(S): Robinson, P.; Hederer, R.
CORPORATE SOURCE: Transplant. Biol. Sect., Clin. Res. Cent., Harrow/Middlesex, HA1 3UJ, UK
SOURCE: Brazilian Journal of Medical and Biological Research (**1994**), 27(2), 263-7
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 10 refs. The authors have examd. intracellular biochem. and metabolic changes induced by **antibodies** specific for **glycosylphosphatidylinositol** (GPI)-anchored cell surface mols. In lymphoid cells the earliest detectable responses are phosphorylation of intracellular substrates. The GPI-linked target antigens are also rapidly redistributed into patches and caps on the cell surface and then internalized. Between two and five hours later, cytokine receptors are expressed. Later, cells become metabolically active and begin to proliferate and express endogenous cytokines, thus promoting autocrine growth. Very early events, such as kinase activity, are induced by antibody binding alone and are characteristic of the cell surface mol. recognized by antibodies. Thus, the initial events in the activation cascade are crit. in selecting the metabolic route. Progression down the activation cascade requires further signals such as crosslinking antibodies, exogenous cytokines, phorbol esters, or accessory cells. Once in cycle, cells no longer display evidence of their original route of activation. Activated T lymphocytes acquire resistance to cleavage by GPI-specific phospholipase C, suggesting a possible feedback mechanism to limit cell proliferation.

L14 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 10
ACCESSION NUMBER: 1994:6423 CAPLUS
DOCUMENT NUMBER: 120:6423
TITLE: Activation of human monocytes and granulocytes by monoclonal **antibodies** to **glycosylphosphatidylinositol**-anchored antigens
AUTHOR(S): Lund-Johansen, Fridtjof; Olweus, Johanna; Symington, Frank W.; Aarli, Aanen; Thompson, John S.; Vilella, Ramon; Skubitz, Keith; Horejsi, Vaclav
CORPORATE SOURCE: Univ. Bergen, Gade Inst., Bergen, Norway
SOURCE: European Journal of Immunology (**1993**), 23(11), 2782-91
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigated possible receptor-like characteristics of glycosylphosphatidylinositol (GPI)-linked antigens on human monocytes and granulocytes by measuring cytoplasmic calcium fluxes and the oxidative burst in cells following crosslinking of GPI-linked antigens. Crosslinking of cell-bound anti-CD14, -CDw52 and -CD55 induced cytoplasmic calcium fluxes and oxidative bursts in unprimed human monocytes similar to those obsd. following Fc.gamma.R crosslinking. In granulocytes primed with 200 nM N-formyl-Met-Leu-Phe (FMLP), crosslinking of cell-bound anti-CD16, -CD24, -CD59 and -CD67 led to calcium fluxes and activation of the oxidative burst. The oxidative bursts mediated by GPI-linked antigens were stronger than those induced by 200 nM FMLP, even though FMLP induced a larger increase in cytoplasmic calcium concn. The responses were likely to be independent of Fc.gamma.R interactions as F(ab')2 fragments of IgG

or IgM antibodies were used in the expts. Activating effects of monoclonal antibody to GPI-linked antigens were not obsd. in cells from patients with paroxysmal nocturnal hemoglobinuria, which are deficient in GPI-linked antigens. In addn., treatment with GPI-specific phospholipase C led to inhibition of cell activation through GPI-linked antigens but not through transmembrane receptors. Crosslinking of a no. of non-GPI-linked antigens (CD11a, CD18, CD31, CD35, CD43, and CD45) neither induced calcium fluxes, nor activated the oxidative burst. The results indicate that most, if not all, GPI-linked surface glycoproteins on myeloid cells are capable of mediating cell activation and suggest that the GPI anchor is a structure facilitating signal transduction.

L14 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:620203 CAPLUS
DOCUMENT NUMBER: 119:220203
TITLE: Rapid purification of glycosyl-phosphatidylinositol-anchored alkaline phosphatase from human neutrophils after up-regulation to the cell surface
AUTHOR(S): Cain, Timothy J.; Liu, Youjiang; Kobayashi, Toshihiro; Robinson, John M.
CORPORATE SOURCE: Dep. Cell Biol. Neurobiol. Anat., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Journal of Histochemistry and Cytochemistry (**1993**), 41(9), 1367-72
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Alk. phosphatase (APase) belongs to a growing family of membrane-assocd. proteins tethered to the lipid bilayer via a glycosyl-phosphatidylinositol (GPI) anchor. Human neutrophils contain an intracellular pool of APase assocd. with a novel membrane-bound compartment. Stimulation of neutrophils with the chemotactic peptide formyl-Met-Leu-Phe (fMLP) leads to rapid up-regulation of essentially all of the APase to sites in continuity with the extracellular medium. Pre-treatment of neutrophils with cytochalasin B (cyto B) followed by fMLP likewise leads to expression of the enzyme on the cell surface and a dramatic alteration in cell morphol., but subsequent internalization of the plasmalemma is minimized. Pre-treatment with cyto B and fMLP has been used for isolation and purifn. of neutrophil APase. Specifically, neutrophils were treated with phosphatidylinositol-specific phospholipase C to release GPI-anchored proteins from the cell surface. APase was purified from supernatants of these prepns. by electrophoresis in a non-denaturing gel system and subsequent electroelution. With this approach the authors rapidly purified neutrophil APase to homogeneity; this protein was then used for immunization. Immunoblotting, ELISA, and immunocytochem. localization were used to characterize the resulting antibodies.

L14 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:406801 CAPLUS
DOCUMENT NUMBER: 119:6801
TITLE: A monoclonal antibody reactive with a glycophosphatidylinositol-anchored molecule on T cells defines CD4+ T cell subsets
AUTHOR(S): Nagata, Norikazu; Taketani, Shigeru; Adachi, Yasushi; Hosaka, Naoki; Miyashima, Shigeo; Tokunaga, Rikio; Ikehara, Susumu
CORPORATE SOURCE: 1st Dep. Pathol., Kansai Med. Univ., Moriguchi, Japan
SOURCE: European Journal of Immunology (**1993**), 23(5), 1193-6
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A hybridoma, 25T3 (IgM, .kappa.), was established from MRL/+ mice immunized with an autoreactive T cell line (1/+ T1). The reactivity of the antigen (Ag) recognized by hybridoma 25T3 (25T3-Ag) expressed on thymic and splenic cells was abolished by treatment with phosphatidylinositol-specific phospholipase C, showing that 25T3-Ag is a glycophosphatidylinositol-anchored Ag. The 25T3-Ag was expressed on approx. 90% of thymocytes. Double-neg., double-pos. and CD8 single-pos. cells were highly pos. for the expression of 25T3-Ag, whereas CD4 single-pos. cells were weakly pos. (approx. 40%) or neg. (approx. 60%). In the spleen, only CD3+ cells (and not B220+ nor Mac-1+ cells) reacted with 25T3 monoclonal antibody (mAb), indicating that 25T3 mAb is specific for T cells. The majority of splenic CD8+ T cells were pos. for the expression of 25T3-Ag, although the intensity was weaker than that of thymocytes. In contrast, splenic CD4+ T cells were divided into neg. (60-70%) and pos. (30-40%) populations. Similar staining profiles were obsd. in BALB/c, C57BL/6, C3H/HeN and AKR/J mice. When BALB/c CD4+ T cell subsets were sorted and cultured with irradiated (25 Gy) antigen-presenting cells, stimulation with immobilized anti-CD3 mAb for 2 days resulted in CD4+25T3+ cells secreting more interleukin-2 and less interleukin-4 than did CD4+25T3- subsets, although the proliferative responses of the cells on day 2 of culture were similar. This suggests that CD4+ T cells can be divided into two populations and relatively defined as T helper 1 and T helper 2 cells using this 25T3 mAb. Immunopptn. and SDS-PAGE revealed that 25T3-Ag was approx. 70 kD. These findings are discussed in relation to CD4+ T cell subsets.

L14 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 11
ACCESSION NUMBER: 1994:5419 CAPLUS
DOCUMENT NUMBER: 120:5419
TITLE: Glycosylphosphatidylinositol-specific phospholipase D is localized in keratinocytes
AUTHOR(S): Xie, Mingsheng; Sesko, Ann M.; Low, Martin G.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: American Journal of Physiology (**1993**), 265(4, Pt. 2), C1156-C1168
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glycosylphosphatidylinositol-specific phospholipase D (GPI-PLD) is abundant in mammalian plasma, but little is known of its cellular and tissue distribution. In this study frozen sections of perfused tissues from adult rats were stained with monoclonal **antibodies** against **GPI-PLD**. The most intense staining was obsd. in the stratified squamous epithelium of the forestomach. Staining was also obsd. in the esophagus, the tongue, the hard palate, and the skin but not in most other tissues including the columnar epithelium of the stomach or the lower gastrointestinal tract. GPI-PLD expression was also detected in several keratinocyte cell lines. Biochem. assays of glycosylphosphatidylinositol-degrading activity using [3H]myristate-labeled variant surface glycoprotein as substrate provided independent

evidence for the presence of GPI-PLD. Expression of GPI-PLD by keratinocytes was not affected by culture in serum-free media, indicating that it does not originate by uptake of serum GPI-PLD in the media. These data suggest that keratinocytes are an important site of action of GPI-PLD and possibly a contributor to the plasma GPI-PLD pool.

L14 ANSWER 30 OF 42 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 12
ACCESSION NUMBER: 94038320 EMBASE
DOCUMENT NUMBER: 1994038320
TITLE: Neutralizing monoclonal **antibodies** to **glycosylphosphatidylinositol**, the dominant TNF-.alpha.-inducing toxin of Plasmodium falciparum: Prospects for the immunotherapy of severe malaria.
AUTHOR: Schofield L.; Vivas L.; Hackett F.; Gerold P.; Schwartz R.T.; Tachado S.
CORPORATE SOURCE: National Inst for Medical Research,Mill Hill, London NW7 1AA, United Kingdom
SOURCE: Annals of Tropical Medicine and Parasitology, (**1993**) 87/6 (617-626).
ISSN: 0003-4983 CODEN: ATMPA2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Tumour necrosis factor-.alpha. (TNF-.alpha.) is an endogenous mediator of shock and inflammation. Many of the life-threatening and severe pathologies associated with complicated and cerebral malaria are thought to result from the overproduction of this cytokine in response to agents of parasite origin. The identification and characterization of these agents may therefore provide the molecular basis for a detailed understanding of the disease process. Recently it has been shown that glycosylphosphatidylinositols are a novel class of glycolipid toxin produced by the parasite, which substitute for the endogenous inositolglycan-based signal transduction pathways of the host. Glycosylphosphatidylinositol stimulates high levels of TNF-.alpha. and interleukin-1 production by macrophages and induces hypoglycaemia through an insulin-mimetic activity, and may therefore contribute to the cerebral syndrome and other malarial pathophysiology. That monoclonal **antibodies** to parasite-derived **glycosylphosphatidylinositol**** * **can neutralize the toxic activities of whole parasite extracts is also demonstrated here. These findings suggest a central role for glycosylphosphatidylinositol of parasite origin in the aetiology of severe malaria and suggest novel approaches for the immunotherapy or immunoprophylaxis of disease.**

L14 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 13
ACCESSION NUMBER: 1993:75619 CAPLUS
DOCUMENT NUMBER: 118:75619
TITLE: Membrane insertion and ***antibody recognition of a **glycosylphosphatidylinositol**-anchored protein: an optical study
AUTHOR(S): Ramsden, J. J.; Schneider, P.
CORPORATE SOURCE: Dep. Biophys. Chem., Biozentrum, Basel, 4056, Switz.
SOURCE: Biochemistry (**1993**), 32(2), 523-9
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetics of binding of a glycolipid-anchored protein (the promastigote surface protease, PSP) to planar lecithin bilayers is studied by an integrated optics technique, in which the bilayer membrane is supported on an optical wave guide and the phase velocities of guided light modes in the wave guide are measured. From these velocities, the optical parameters of the membrane and PSP layers deposited on the wave guide are detd., yielding in particular the mass of PSP bound to the membrane, which is followed in real time. From a comparison of the binding rates of PSP and PSP from which the lipid moiety has been removed, it is shown that the lipid moiety plays a key role in anchoring the protein to the membrane. Specific and nonspecific binding of antibodies to membrane-anchored PSP is also investigated. As little as a fifth of a monolayer of PSP is sufficient to suppress the appreciable nonspecific binding of antibodies to the membrane.

L14 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:629485 CAPLUS
DOCUMENT NUMBER: 117:229485
TITLE: Immunolocalization of a glycosylphosphatidylinositol-specific phospholipase D in mast cells found in normal tissue and neurofibromatosis lesions
AUTHOR(S): Metz, Christine N.; Thomas, Patricia; Davitz, Michael A.
CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, USA
SOURCE: American Journal of Pathology (**1992**), 140(6), 1275-81
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A large no. of eukaryotic proteins have been shown to be anchored to the cell membrane by glycosylphosphatidylinositol (GPI). This glycolipid anchor can serve as a substrate for anchor-specific phospholipases that convert the GPI-anchored membrane proteins into sol. forms. Sol. forms of many GPI anchored proteins have been identified in vivo in connective tissue, plasma, and urine. The authors have discovered that mammalian plasma contains a GPI-specific phospholipase D (GPI-PLD). Because it recognizes a portion of the conserved glycan core structure, all GPI-anchored proteins are potential substrates. The authors report the development of a murine monoclonal antibody specific for one form of the human GPI-PLD and the immunohistochem. localization of this enzyme to mast cells.

L14 ANSWER 33 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:462022 BIOSIS
DOCUMENT NUMBER: BR43:83372
TITLE: PAROXYSMAL NOCTURNAL HEMOGLOBINURIA DIAGNOSIS WITH THE FLUORESCENCE-ACTIVATED CELL SORTER.
AUTHOR(S): SCHUBERT J; SCHMIDT R E
CORPORATE SOURCE: ABT. KLINISCHE IMMUNOL., ZENTRUM INNERE MED. DERMATOL., MEDIZINISCHE HOCHSCHULE, KONSTANTY-GUTSCHOW-STR. 8, W-3000 HANNOVER 61.
SOURCE: DMW, Dtsch. Med. Wochenschr., (1992) 117 (25), 985-989.
CODEN: DDMWDF. ISSN: 0012-0472.

FILE SEGMENT: BR; OLD
LANGUAGE: German

L14 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:468166 CAPLUS
DOCUMENT NUMBER: 117:68166
TITLE: Purification and characterization of **antibodies** to the **glycosylphosphatidylinositol** anchor of human membrane dipeptidase
AUTHOR(S): Broomfield, Samantha J.; Hooper, Nigel M.
CORPORATE SOURCE: Dep. Biochem. Mol. Biol., Univ. Leeds, Leeds, LS2 9JT, UK
SOURCE: Biochemical Society Transactions (**1992**), 20(2), 118S
CODEN: BCSTB5; ISSN: 0300-5127
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By affinity chromatog. on immobilized phosphatidyinositol-specific phospholipase C solubilized aminopeptidase P, a cross-reacting determinant (CRD)-specific antiserum, RH177/S, was purified from a crude antiserum raised to the phosphatidyinositol-specific phospholipase C solubilized form of human kidney dipeptidase. This antiserum was shown, by Western blotting and an ELISA, to recognize other G-PI anchored proteins, the major epitope being the inositol 1,2-monophosphate formed on phospholipase C cleavage of the anchor. Recognition by RH177/S may also involve a minor epitope, possibly a substituent on the inositol ring or the glucosamine residue which is resistant to mild acid treatment. Purifn. of CRD-specific antibodies by a second method with membrane-form dipeptidase immobilized on nitrocellulose was unsuccessful.

L14 ANSWER 35 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:468061 BIOSIS
DOCUMENT NUMBER: BR43:89411
TITLE: MONOCLONAL **ANTIBODIES** AGAINST **GLYCOSYLPHOSPHATIDYLINOSITOL**-SPECIFIC PHOSPHOLIPASE D.
AUTHOR(S): LIAO J; HONER M; MORTENSEN V; KOCH C; NORGAARD-PEDERSEN B; BRODBECK U
CORPORATE SOURCE: INSTITUTE BIOCHEMISTRY MOLECULAR BIOLOGY, UNIVERSITY BERN, SWITZ.
SOURCE: 24TH ANNUAL MEETING OF THE SWISS SOCIETIES FOR EXPERIMENTAL BIOLOGY (USGEB/USSBE), BASEL, SWITZERLAND, MARCH 19-20, 1992. EXPERIENTIA (BASEL), (1992) 48 (ABSTR), A19.
CODEN: EXPEAM. ISSN: 0014-4754.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L14 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:629904 CAPLUS
DOCUMENT NUMBER: 115:229904
TITLE: Evidence of synergy between Thy-1 and CD3/TCR complex in signal delivery to murine thymocytes for cell death
AUTHOR(S): Nakashima, Izumi; Zhang, Yue Hua; Rahman, S. M. Jamshedur; Yoshida, Tomoaki; Isobe, Kenichi; Ding, Linna; Iwamoto, Takashi; Hamaguchi, Michinari; Ikezawa, Hiroh; Taguchi, Ryo
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Journal of Immunology (**1991**), 147(4), 1153-62
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The potential role of Thy-1 in CD3/TCR complex-mediated signal delivery to murine thymocytes was studied. Antigen (Ag)-mimicking cross-linked anti-CD3 mAb stimulated suspension of thymocytes from adult (6-8 wk old) mice for a brisk free cytoplasmic calcium ion ([Ca2+]i) rise, low level of inositol phosphate prodn., and marginal increase in tyrosine-specific phosphorylation of 110/120-kDa and 40-kDa cellular proteins. Weak but sustained [Ca2+]i rise, low inositol phosphate prodn., and weak protein tyrosine phosphorylation were also induced by the cross-linked anti-Thy-1 mAb that mimicked the putative natural ligand. The signal delivered via either of these two pathways was however insufficient for definitively promoting cell death and DNA fragmentation in the adult thymocytes. Here it is demonstrated that anti-Thy-1 mAb synergized with anti-CD3 mAb for inducing a long-lasting prominent [Ca2+]i rise, definite inositol 1,4,5-triphosphate and inositol 1,3,4,5-tetrakiphosphate prodn., and extensive tyrosine-specific phosphorylation of 110/120-, 92-, 75-, and 40-kDa proteins, which resulted in marked promotion of cell death and DNA fragmentation in the adult thymocytes. This unique anti-Thy-1 **antibody** activity was directed to **glycosylphosphatidylinosito** 1-anchored Thy-1, and was distinguished from the known anti-L3T4 activity that augmented the CD3-mediated signal transduction in a different manner. The synergistic actions of anti-CD3 and anti-Thy-1 mAb obligatorily required the crosslinking of the two mAb together. The anti-CD3 and anti-Thy-1 mAb cross-linked together acted on immature thymocytes from newborn (<24 h after birth) mice for more extensive promotion of protein tyrosine phosphorylation and cell death. In addn., they affected peripheral T lymphocytes for accelerating protein tyrosine phosphorylation but not cell death. These results suggest a novel function of glycosylphosphatidylinositol-anchored Thy-1 as a possible unique intrathymic intensifier of the CD3/TCR complex-delivered signal for neg. thymocyte selection.

L14 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:18698 CAPLUS
DOCUMENT NUMBER: 116:18698
TITLE: Signal transduction by GPI-anchored membrane proteins
AUTHOR(S): Robinson, Peter J.
CORPORATE SOURCE: Transplant. Biol. Sect., Clin. Res. Cent., Harrow, UK
SOURCE: Cell Biology International Reports (**1991**), 15(9), 761-7
CODEN: CBRPDS; ISSN: 0309-1651
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 16 refs., of the role of glycosyl-phosphatidylinositol (GPI)-anchored membrane proteins and antibodies to them in signal transduction. Functions of GPI anchors, their role in activation of lymphocytes, mol. assocns. on the cell surface involving these anchors, and cell surface mobility and signaling are topics included.

L14 ANSWER 38 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1991:136813 BIOSIS
DOCUMENT NUMBER: BA91:73353
TITLE: CHARACTERIZATION OF **ANTIBODIES** TO THE **GLYCOSYLPHOSPHATIDYLINOSITOL** MEMBRANE ANCHORS OF MAMMALIAN PROTEINS.
AUTHOR(S): HOOPER N M; BROOMFIELD S J; TURNER A J
CORPORATE SOURCE: MEMBRANE PEPTIDASE RES. GROUP, DEP. BIOCHEM. AND MOLECULAR BIOL., UNIV. LEEDS, LEEDS LS2 9JT, UK.
SOURCE: BIOCHEM J, (1991) 273 (2), 301-306.
CODEN: BIJOAK. ISSN: 0306-3275.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Two polyclonal antisera were raised in rabbits to the phospholipase C-solubilized forms of pig renal dipeptidase (EC 3.4.13.11) and pig aminopeptidase P (EC 3.4.11.9). These antisera were purified and shown to cross-react with other glycosyl-phosphatidylinositol (G-PI)-anchored proteins isolated from pig, human and trypanosomes. The epitopes involved in this cross-reactivity were characterized by Western-blot analysis after mild acid or nitrous acid treatment of the G-PI-anchored proteins and by a competitive (ELISA) with other G-PI-anchored proteins and individual components of the anchor structure. These studies revealed that the primary epitope for both antisera is the inositol 1,2-(cyclic)monophosphate that is formed on phospholipase C cleavage of the intact G-PI anchor. Other minor epitopes, such as phosphoethanolamine, probably involve side-chain modifications to the core anchor structure that may be species-specific.

L14 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 14
ACCESSION NUMBER: 1991:605569 CAPLUS
DOCUMENT NUMBER: 115:205569
TITLE: Production of monoclonal **antibodies** against the purified **glycosylphosphatidylinositol** anchor of the variant surface glycoprotein from Trypanosoma brucei brucei
AUTHOR(S): Preuss, Ute; Schuler, Frank; Peter-Katalinic, Jasna; Gunawan, Johannes; Egge, Heinz
CORPORATE SOURCE: Inst. Physiol. Chem., Univ. Bonn, Bonn, W-5300/1, Germany
SOURCE: Archives of Biochemistry and Biophysics (**1991**), 291(1), 139-46
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The glycosylphosphatidylinositol anchor (GPI) from the membrane form variant surface glycoprotein (mfVSG) of T. brucei brucei was isolated and identified after radioactive labeling with [3H]myristic acid, by immunostaining on HPTLC with a polyclonal antibody directed against mfVSG, and by neg. ion laser desorption and fast atom bombardment mass spectrometry of the GPI anchor before and after peracetylation. For the prodn. of monoclonal antibodies the purified GPI mol. was incorporated into liposomes and injected intrasplenically in BALB/c mice. After fusion with the myeloma cell line X63-Ag 8.653 hydridoma cells were cloned by single cell cloning. The secreted antibodies were characterized by ELISA, Ouchterlony immunodiffusion, and Western blot and used in first immunofluorescent studies.

L14 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:513461 CAPLUS
DOCUMENT NUMBER: 113:113461
TITLE: Production and characterization of antibodies against the cross-reacting determinant of glycosyl-phosphatidylinositol-anchored acetylcholinesterase
AUTHOR(S): Jaeger, Karin; Meyer, Pascale; Stieger, Susi; Brodbeck, Urs
CORPORATE SOURCE: Inst. Biochem. Molekularbiol., Univ. Bern, Bern, Switz.
SOURCE: Biochimica et Biophysica Acta (**1990**), 1039(3), 367-73
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dimeric acetylcholinesterase is anchored in the cell membrane by a glycosylphosphatidylinositol attached to the C-terminus of the protein. The complex glycan contains an antigenic epitope, the cross-reacting determinant (CRD), which is only revealed after removal of the diradylglycerol by phosphatidylinositol-specific phospholipase C (PI-PLC) but is cryptic in the amphiphilic form. Polyclonal antibodies were raised against the CRD of vertebrate acetylcholinesterase. The purified anti-CRD antibodies recognized only the PI-PLC treated hydrophilic forms of acetylcholinesterase. The purified anti-CRD antibodies recognized only the PI-PLC treated hydrophilic forms of acetylcholinesterase from bovine erythrocytes and Torpedo, and of variant surface glycoproteins from trypanosomes but not the corresponding amphiphilic proteins. Competition expts. showed that inositol-1,2-cyclic phosphate and glucosamine inhibited the binding of the antibodies to the CRD. Furthermore, binding of the anti-CRD antibodies to acetylcholinesterase contg. N-methylated glucosamine was markedly reduced. The amphiphilic N-methylated enzyme is less sensitive to digestion with PI-PLC than the nonmethylated form. Thus, inositol-1,2-cyclic phosphate and glucosamine, esp. the free amine group of this residue, contribute significantly to the epitope recognized by the anti-CRD antibodies.

L14 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 15
ACCESSION NUMBER: 1989:592936 CAPLUS
DOCUMENT NUMBER: 111:192936
TITLE: **Antibodies** to 5'-nucleotidase (CD73), a **glycosylphosphatidylinositol**-anchored protein, cause human peripheral blood T cells to proliferate
AUTHOR(S): Thompson, Linda F.; Ruedi, Julie M.; Glass, Alison; Low, Martin G.; Lucas, Alexander H.
CORPORATE SOURCE: Dep. Immunol., Scripps Clin. Res. Found., La Jolla, CA, 92037, USA
SOURCE: J. Immunol. (**1989**), 143(6), 1815-21
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human peripheral blood T cells were stimulated to proliferate when cultured with submitogenic doses of PMA and goat antibodies to 5'-nucleotidase (5'-NT). The degree of proliferation, as measured by [3H]TdR incorporation on day 3, was similar to that achieved by stimulation with PHA. Anti-5'-NT antibodies had no effect on PHA-induced proliferation. Maximal stimulation was achieved with 0.6-1.0 ng/mL of PMA and 125 .mu.g/mL of IgG isolated from a goat anti-5'-NT antiserum. Both

intact IgG and F(ab')2 fragments were stimulatory. Interleukin 2 receptor expression and IL-2 secretion were also induced by anti-5'-NT antibodies and PMA. Anti-5'-NT-induced proliferation was inhibited >95% by a murine anti-IL-2 receptor mAb and required <0.3% monocytes. Similar results were obtained with a murine mAb specific for 5'-NT. As expected, anti-5'-NT antibodies and PMA did not induce the proliferation of ecto-5'-NT-T cells isolated by cell sorting. Pretreatment of total T cells with phosphatidylinositol-specific phospholipase C removed an av. of 89% of the 5'-NT activity from the cell surface and also inhibited by 83% the ability of the cells to proliferate in response to anti-5'-NT antibodies and PMA. Thus, the activation signal provided by anti-5'-NT antibodies is apparently transduced, in large part, by a form of the enzyme that is attached to the membrane via glycosyl-phosphatidylinositol linkage. The 5'-NT may play a role in lymphocyte activation as has been proposed for other glycosyl-phosphatidylinositol-anchored lymphocyte surface proteins.

L14 ANSWER 42 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1990:70518 BIOSIS
DOCUMENT NUMBER: BA89:38344
TITLE: MOLECULAR CHARACTERIZATION OF BABESIA-BOVIS MEROZOITE SURFACE PROTEINS BEARING EPITOPES IMMUNODOMINANT IN PROTECTED CATTLE.
AUTHOR(S): HINES S A; MCELWAIN T F; BUENING G M; PALMER G H
CORPORATE SOURCE: DEP. VET. MICROBIOL. PATHOL., WASHINGTON STATE UNIV., PULLMAN, WASH. 99164-7030.
SOURCE: MOL BIOCHEM PARASITOL, (1989) 37 (1), 1-10.
CODEN: MBIPDP. ISSN: 0166-6851.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Eight surface-radioiodinated merozoite proteins from a cloned, pathogenic isolate of Babesia bovis can be immunoprecipitated by antibody from cattle that are completely against clinical babesiosis. Among these eight surface proteins, the 55- and 42-kDa molecules are biosynthetically labeled with [3H]glucosamine. The 42-kDa glycoprotein can also be labeled with [3H]myristic acid and partitions exclusively into the detergent phase in Triton X-114 extracts, indicating that it is an integral membrane protein and suggesting that it is anchored by a **glycosylphosphatidylinositol* ** moiety. ***Antibody**-mediated protection against B. bovis merozoites most probably requires a high level of circulating antibody to ensure antibody-merozoite binding during the parasite's brief extraerythrocytic phase. Antibodies in diluted sera selectively recognize the 120-, 85-, 55- and 42-kDa surface proteins. Only the 42-kDa integral membrane protein is reactive with serum antibodies diluted .gtoreq. 1:16 000. Thus, we hypothesize that these immunodominant proteins, especially the transmembrane 42-kDa glycoprotein, are important to the induction of the protective immune response and are candidates for an improved vaccine against babesiosis.

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(FILE 'HOME' ENTERED AT 16:59:18 ON 15 OCT 2002)

FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 16:59:34 ON 15 OCT 2002
L1 550 S RADEMACHER T?/AU OR WHITBY H?/AU
L2 47 S L1 AND (IPG OR (INOSITOLPHOSPHOGLYCANS))
L3 28 DUP REM L2 (19 DUPLICATES REMOVED)
L4 1 S L3 AND GPI-PLD
L5 1504 S (IPG OR (INOSITOLPHOSPHOGLYCAN?))
L6 4 S L5 (P) (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL (1N) PHOSP
L7 3 DUP REM L6 (1 DUPLICATE REMOVED)
L8 80 S L5 (10N) ANTIBOD?
L9 51 S L8 AND PD<19980327
L10 25 DUP REM L9 (26 DUPLICATES REMOVED)
L11 9525 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL))
L12 122 S (GPI-PLD OR (GLYCOSYLPHOSPHATIDYLINOSITOL)) (5N) ANTIBOD?
L13 67 S L12 AND PD<19980327
L14 42 DUP REM L13 (25 DUPLICATES REMOVED)
L15 0 S L14 (10N) ADMINIST?
L16 0 S L14 (P) ADMINIST?

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